Application No. (if known): 09/467,317 Attorney Docket No.: 20052/1200517-US3

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RANDOLPH J. NOELLE, Appellant, v. SETH LEDERMAN, LEONARD CHESS, and MICHAEL J. YELLIN, Appellees.

02-1187

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

2004 U.S. App. LEXIS 774

January 20, 2004, Decided

PRIOR HISTORY: [*1] Appealed from: United States Patent and Trademark Office Board of Patent Appeals and Interferences. (Interference No. 104,415). *Noelle v. Lederman, 2001 Pat. App. LEXIS 8 (Bd. Pat. App. & Interferences, Oct. 19, 2001)*

DISPOSITION: AFFIRMED.

LexisNexis (TM) HEADNOTES - Core Concepts:

COUNSEL: E. Anthony Figg, Rothwell, Figg, Ernst & Manbeck, of Washington, DC, argued for appellant. With him on the brief was Glenn E. Karta.

James F. Haley, Jr., Fish & Neave, of New York, New York, argued for appellees. With him on the brief were Margaret A. Pierri and Jane T. Gunnison. Of counsel on the brief was John P. White, Cooper & Dunham LLP, of New York, New York. Of counsel was Stanley Den-Kua Liang, Fish & Neave.

JUDGES: Before CLEVENGER, BRYSON, and GAJARSA, Circuit Judges.

OPINIONBY: GAJARSA

OPINION: GAJARSA, Circuit Judge.

This is an appeal from an interference proceeding involving the claims of United States Patent Application Serial No. 08/742,480 (the "'480 application") and *United States Patent No. 5,474,771* (the "'771 patent"). Randolph J. Noelle ("Noelle") is the inventor named on the '480 application. Seth Lederman, Leonard Chess, and Michael J. Yellin (collectively "Lederman") are the inventors named on the '771 patent. Noelle appeals the decision of the United States Patent and Trademark Office, Board of Patent Appeals and Interferences [*2] ("Board"), finding no interference-in-fact between the '480 application and the '771 patent and rejecting claims 51, 52, 53, 56, 59, and 60 of the '480 application pursuant to *35 U.S.C. § 102(b) (2000)*. Noelle v. Lederman, Interference No. 104,415 (Bd. Pat. App. & Int. Oct. 19, 2001). Because the decision of the Board is supported by substantial evidence and is not contrary to law, we affirm.

BACKGROUND

A. Antibodies

This case relates to antibodies and their role in the immune response system. A vertebrate's immune system serves to identify and destroy foreign invading organisms and neutralize the toxic molecules they produce. Antibodies, which are proteins also referred to as immunoglobulins ("Ig"), serve to designate foreign particles, broadly referred to as antigens, for destruction by other components of the immune system such as lymphocytes. n1 Lymphocytes, otherwise known as white blood cells, produce antibodies and destroy antigens. T-cells and B-cells are the two types of lymphocytes needed for antibody production. One specific type of T-cell is the helper T-cell. Helper T-cells recognize antigens and then induce B-cells to produce antibodies [*3] through a series of events. First the helper T-cell is activated after it recognizes an antigen. Once activated, the helper T-cell activates the B-cell by a combination of binding with the B-cell and secreting signaling molecules. Once the B-cell is activated, it differentiates, n2 proliferates, and produces antibodies specific to a particular antigen. The antibodies then circulate in the bloodstream and permeate other bodily

fluids, where they bind to the antigen, thereby flagging it for destruction.

n1 For additional background on the function of antibodies, as well as methods of isolating antibodies, see *In re Wands, 858 F.2d 731, 733-34 (Fed. Cir. 1988)* and *Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1368-69 (Fed. Cir. 1986).*

n2 Cell differentiation is the process of modifying a cell's structure and function in order for it to become more specialized and specific to the invading antigen.

The present interference involves competing claims to an antibody **[*4]** ("CD40CR antibody") that represses the cell-to-cell signaling interaction between helper T-cells and B-cells. CD40CR antigen n3 is found on activated, but not resting, helper T-cells. CD40CR antigen acts as a "key" to unlock a protein ("CD40") located on the surface of resting B-cells. Once CD40CR antigen and CD40 bind, the B-cell begins down the pathway to differentiation, proliferation, and antibody production. The CD40CR antibody binds to the CD40CR antigen located on the T-cell surface, thereby inhibiting its ability to bind to the CD40 receptor located on the resting B-cell. B-cells cannot then become activated, thereby preventing the B-cell from producing antibodies. CD40CR antibodies are useful for treating a hyperactive immune system that causes allergic reactions and autoimmune diseases.

n3 CD40CR antigen is also referred to as "CD40 counter receptor," "CD40 ligand," "CD40L," and simply "CD40CR." Lederman uses the term "5c8 antigen" or "T-B cell-activating molecule" ("T-BAM") to designate the 30-kilodalton human form of CD40CR antigen. Noelle uses the term "gp39" (glycoprotein 39 kD) to describe the 39-kilodalton mouse form of CD40CR antigen.

[*5]

B. The Interference

Noelle's '480 application was filed November 1, 1996. The '480 application is a continuation of application Serial No. 08/338,975 ("the '975 application"), filed November 14, 1994, which is in turn a continuation of application Serial No. 07/835,799 ("the '799 application"), filed on February 14, 1992. The claims of Noelle's '480 application are directed to the genus, murine ("mouse"), chimeric ("hybrid"), humanized, and human forms of the CD40CR monoclonal antibody. Noelle also claims the hybridomal n4 cell lines that produce the CD40CR antibody.

n4 A hybridoma is a man-made tissue culture consisting of cancerous B-cells fused to B-cells producing the antibody of choice. A hybridoma produces unlimited amounts of a desired "monoclonal" antibody. See *Hybritech, 802 F.2d at 1368-69* (explaining the method for creating and using hybridomas).

Lederman's '771 issued patent has an effective filing date of November 15, 1991. Lederman's '771 patent describes and claims the **[*6]** human form of CD40CR monoclonal antibody (the "5c8 antibody"). The 5c8 antibody binds to "the 5c8 antigen located on the surface of activated T cells and thereby inhibits T cell activation of B cells." Also, Lederman claims a hybridomal cell line created to produce monoclonal antibody 5c8.

On September 3, 1999, an interference was declared by the United States Patent and Trademark Office ("USPTO") between the issued claims of Lederman's '771 patent and Noelle's '480 application. Noelle was designated the junior party and Lederman was designated the senior party based on their effective filing dates. The USPTO established only one count in the interference. The count reads as follows:

> The monoclonal antibody of claim 1 of *5,474,771* or the monoclonal antibody of claim 42 or claim 51 of 08/742,480.

Claim 1 of Lederman's '771 patent reads as follows:

> A monoclonal antibody, which specifically binds and forms a complex with the 5c8 antigen located on the surface of activated T cells and thereby inhibits T cell activation of B cells, the 5c8 antigen being an antigen to which monoclonal antibody 5c8 (ATCC Accession No. HB 10916) specifically binds.

Claim 42 of Noelle's **[*7]** '480 application reads as follows:

> A monoclonal antibody or fragment thereof which specifically binds to an antigen expressed on activated T cells, wherein said antigen is specifically bound

> by the monoclonal antibody secreted by hybridoma MR1 which hybridoma has been deposited and accorded ATCC Accession No. HB 11048.

Claim 51 of Noelle's '480 application reads as follows:

> A monoclonal antibody or fragment thereof which specifically binds CD40CR.

Claim 52 of Noelle's '480 application reads as follows:

> The monoclonal antibody or fragment of Claim 51, wherein said CD40CR is expressed by activated human T cells.

For sake of the simplicity, Claim 1 of Lederman's '771 patent and Claim 52 of Noelle's '480 application will be referred to as claims to the "human" form of CD40CR antibody. Claims 42 and 51 of Noelle's '480 application will be referred to as claims to the "mouse" and "genus" forms of CD40CR antibody, respectively.

On June 28, 2001 the Board held a hearing to dispose of the parties' preliminary motions. Lederman moved to have Noelle's claims rejected and sought to redefine the count. Likewise, Noelle also sought to have the count redefined. **[*8]** The Board denied Lederman's motions for judgment against Noelle's mouse claims for lack of written description, lack of enablement, and indefiniteness. See *35 U.S.C. § 112 (2000)*. The Board found that Lederman had failed to demonstrate that the mouse claims in Noelle's '480 application failed to comply with *35 U.S.C. § 112*, paragraphs (1) and (2), as of November 1, 1996, the date Noelle filed his '480 application. The Board, however, determined that the human and genus claims in Noelle's '480 application failed to comply with the written description requirement pursuant to *35 U.S.C. § 112*, paragraph (1), as of February 14, 1992, the date Noelle filed the previous '799 application. The Board made a detailed analysis of this court's precedent pertaining to the doctrine of written description, focusing on the holding from Regents of the University of California v. Eli Lilly & Co. that an "adequate written description of a DNA sequence claim requires a precise definition, such as structure, formula, chemical name, or physical properties." *119 F.3d 1559, 1566 (Fed. Cir. 1997)*. The Board analogized **[*9]** the DNA claims from Regents to the antibodies in Noelle's application. Accordingly, the Board held that Noelle's claims regarding the genus and human claims from the '480 application lacked written description support in the specification of Noelle's earlier '799 application because Noelle failed to describe any structural features of the human or genus antibodies or antigens. In other words, the Board found that the claims covering the genus and human antibodies constituted new matter because they lacked adequate written description in Noelle's earlier '799 application. The Board did not reject the claims, but rather denied them the benefit of the earlier filing date of Noelle '799.

Next, the Board addressed the implication of finding a lack of written description for the genus and human claims in Noelle's '480 application. The Board determined that the claims to the human and genus forms of CD40CR antibody in Noelle's '480 application were anticipated by either Lederman '771, which claims priority to U.S. Application 07/792,728, filed November 15, 1991, or Armitage 5,961,974 (the "'974 patent"), which claims priority to U.S. applications 07/783,707 and 07/805,723 filed October 25, 1991, and **[*10]** December 5, 1991, respectively. Noelle had not attempted to distinguish his human and genus claims from the prior art and had conceded that Lederman '771 and Armitage '974 would anticipate those claims if the '480 application were not afforded the earlier filing date of Noelle's '799 application. Thus, the Board found the genus and human claims of Noelle's '480 application to be anticipated under *35 U.S.C. § 102(b)* by the two forms of prior art and, as a result, rejected the claims to the human and genus forms of CD40CR antibodies and their respective cell lines pursuant to *37 C.F.R. § 1.641*.

On October 19, 2001, the Board ruled on the motions remaining from the previous hearing. The Board had determined in its previous hearing that the deferred motions were essentially requests to decide whether an interference-in-fact existed between the two parties' claims. Lederman then withdrew his pending motions and filed a new motion requesting that the Board find no interference-in-fact.

The Board concluded from the evidence submitted that there was no interference-in-fact. The Board reasoned that a person of ordinary skill in the art lacked **[*11]** a reasonable expectation of success of obtaining the other party's claimed invention given the state of the art at the time. The Board noted three different methods disclosed in Noelle's '480 specification by which a person of ordinary skill in the art could have isolated the human form of the CD40CR antibody given the mouse version of the CD40CR antibody. Dr. Edward A. Clark, Noelle's expert, declared that a person skilled in the art would have had a reasonable expectation of success in isolating human CD40CR antibody by utilizing the methods disclosed in Noelle's specification.

First, Clark testified that human CD40CR antibody could be isolated by immunizing a host with human CD40CR antigen expressing cells or cell lines and selecting the antibody to the CD40CR antigen by

functional or competition binding with CD40-Ig. n5 Next, Clark suggested methods of making and isolating antibodies using affinity purified human CD40CR antigen. Last, Dr. Clark declared that one skilled in the art could use the mouse CD40CR antibody or CD40-Ig to clone CD40CR antigen DNA using a method known as expression cloning.

> n5 CD40-Ig is a fusion protein wherein a portion of the CD40 receptor is fused to an immunoglobulin (Ig). CD40-Ig is therefore not expressed on the surface of a B-cell but rather is essentially a soluble, free-floating molecule.

[*12]

The Board found that one skilled in the art would not have had a reasonable expectation of success of isolating human CD40CR antibodies given the mouse form of CD40CR antigen. At the outset, the Board reasoned that any reference to Noelle's own specification as prior art was improper because the specifications underlying the respective claims cannot be considered "prior art" and an interference-in-fact analysis requires the comparison between the parties' claims, not their specifications. *In re Vaeck, 947 F.2d 488, 493 (Fed. Cir. 1991)*. Nevertheless, the Board refuted the three methods disclosed in Noelle's specification and endorsed by Clark. First, the Board found that the immunization technique found in the prior art would be ineffective because, at the relevant time, one skilled in the art would not have had a reasonable expectation of success of identifying the activated T-cells that produced the required CD40CR antigen or of isolating the antigen itself. Second, the Board found that it would have been "extremely difficult" for a person of ordinary skill in the art to isolate successfully CD40-Ig, which, as Noelle asserted, could then be used to obtain the claimed **[*13]** CD40CR antibodies. Third, the Board cited statements made during the prosecution of Armitage application 07/969,703 for the proposition that a skilled artisan could not have used expression cloning to isolate CD40CR antibody with a reasonable likelihood of success.

Thus, the Board determined that a person of ordinary skill in the art would not have been reasonably likely to isolate human CD40CR antibody given Noelle's claimed invention of mouse CD40CR antibody. As a result, the Board found no interference-in-fact between Noelle's remaining murine CD40CR antibody claim and Lederman's claim to the human form of CD40CR antibody. Noelle timely appealed to this court and we have jurisdiction under *28 U.S.C. § 1295(a)(4)(A) (2000)*.

DISCUSSION

Whether a specification complies with the written description requirement of *35 U.S.C. § 112*, paragraph (1), is a question of fact, *Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1562 (Fed. Cir. 1991)*, and is, in appeals from the Board, reviewed under the substantial evidence standard. *In re Gartside, 203 F.3d 1305, 1315 (Fed. Cir. 2000)*. To apply a substantial evidence **[*14]** standard, this court must "examine the record as a whole, taking into account evidence that both justifies and detracts from an agency's decision." *Id. at 1312*. A reviewing court must ask "whether a reasonable fact finder could have arrived at the agency's decision." Id. "The possibility of drawing two inconsistent conclusions from the evidence does not prevent an administrative agency's finding from being supported by substantial evidence." Id.

A. Entitlement to Priority

The written description requirement has been defined many times by this court, but perhaps most clearly in Vas-Cath. The court held as follows:

> *35 U.S.C. § 112*, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is **[*15]** now claimed.

Vas-Cath, 935 F.2d at 1563-64 (emphasis in original). Thus, the test to determine if an application is to receive the benefit of an earlier filed application is whether a person of ordinary skill in the art would recognize that the applicant possessed what is claimed in the later filed application as of the filing date of the earlier filed application. An earlier application that describes later-claimed genetic material only by a statement of function or result may be insufficient to meet the written description requirement. See *Regents of Univ. of Cal. v. Eli Lilly & Co. , 119 F.3d 1559, 1566.* This court has held that a description of DNA "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. (quoting *Fiers v. Revel, 984 F.2d 1164, 1170 (Fed. Cir. 1993))*. Therefore, this court has held that statements in the specification describing the functional characteristics of a DNA molecule or methods of its isolation do not

adequately describe a particular claimed DNA sequence. Instead "an adequate written description of DNA requires **[*16]** more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id. at 1566-67* (quoting *Fiers, 984 F.2d at 1171*). It should be noted, however, that this court in Vas-Cath warned that each case involving the issue of written description, "must be decided on its own facts. Thus, the precedential value of cases in this area is extremely limited." *Vas-Cath, 935 F.2d at 1562* (quoting *In re Driscoll, 562 F.2d 1245, 1250 (C.C.P.A. 1977))*.

Indeed, the court in *Enzo Biochem v. Gen-Probe, Inc., 323 F.3d 956, 964 (Fed. Cir. 2002)* ("Enzo Biochem II"), stated that "the written description requirement would be met for all of the claims [of the patent at issue] if the functional characteristic of [the claimed invention was] coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed." Also, the court held that one might comply with the written description requirement by depositing the biological material with a public depository such as the American Type Culture **[*17]** Collection ("ATCC"). *Id. at 970*. The court proffered an example of an invention successfully described by its functional characteristics. The court stated:

> For example, the PTO would find compliance with 112, paragraph 1, for a claim to an isolated antibody capable of binding to antigen X, notwithstanding the functional definition of the antibody, in light of the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature.

Id. The court adopted the USPTO Guidelines as persuasive authority for the proposition that a claim directed to "any antibody which is capable of binding to antigen X" would have sufficient support in a written description that disclosed "fully characterized antigens." Synopsis of Application of Written Description Guidelines, at 60, available at http://www.uspto.gov/web/menu/written.pdf (last visited Jan. 16, 2003) (emphasis added).

Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical **[*18]** name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen.

Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the **[*19]** "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

Moreover, Noelle cannot claim the genus form of CD40CR antibody by simply describing mouse CD40CR antigen. Noelle cites *Staehelin v. Secher, 24 U.S.P.Q.2d 1513, 1519* (Bd. Pat. App. & Int. Sept. 28, 1992), as support for his argument that he has rights to the genus form of CD40CR antibody. In Staehelin, Dr. Secher had developed a hybridoma that produced a monoclonal antibody targeted to an antigen unavailable in pure form. Id. The antigen was human leukocyte interferon. Id. In Secher's foreign application, he had reported the isolation of a hybridoma-secreting antibody to human leukocyte interferon. Id. In his subsequent U.S. application, Secher claimed the genus form of the antibody. *Id. at 1520*. The Board held, "Secher's disclosure . . . would have reasonably conveyed to a person possessing **[*20]** ordinary skill in the art that Secher possessed the genus later claimed by them in their U.S. application in the sense of *35 U.S.C. 112*, first paragraph." Id. The Board held it is not necessary to describe the exact details for preparing every species within the genus in order to claim the genus. Id. (citing *Utter v. Hiraga, 845 F.2d 993, 998 (Fed. Cir. 1988))*. Thus, Noelle argues, the disclosure in his previous '799 application of the mouse form of CD40CR antibody was sufficient to support his later genus claims.

Noelle's reliance on *Staehelin* is misplaced. First, it is a decision from the Board of Patent Appeals and Interferences which may be persuasive but it is not binding precedent on this court. Second, the Board in Staehelin cited Utter to support the proposition that a patentee need not cite every species of an antibody in order to claim the genus of that antibody. In Utter, this court held that not every species of scroll compressor used in air conditioners must be described in order for a genus claim to meet the written description requirement. *845 F.2d at 994*. Since the Board's decision in Staehelin **[*21]** , this court has subsequently held that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Enzo Biochem II, 323 F.3d at 965*; *Regents, 119 F.3d at 1568*. Therefore, to the extent the Board's decision in *Staehelin* conflicts with our decisions in Enzo Biochem II and Regents, it has been limited in applicability.

The Board was also correct in its determination that the human and genus claims were anticipated by Lederman '771 and Armitage '974. The Board's decision was supported by substantial evidence, and Noelle conceded that without the earlier filing date of his '799 application, his claims were indistinguishable from the prior art cited by the Board.

B. Interference-In-Fact

Interference proceedings are subjected to the requirements of *37 C.F.R. § § 1.601 - 1.690* (2003), promulgated pursuant to *35 U.S.C. § 135(a)*. *Eli Lilly v. Bd. of Regents of the Univ. of Wash., 334 F.3d 1264, 1267 (Fed. Cir. 2003)*. **[*22]** A patent interference is designed to "determine whether two patent applications (or a patent application and an issued patent) are drawn to the same 'patentable invention' and, if so, which of the competing parties was first to invent the duplicative subject matter." *Id.* (citing *Conservolite, Inc. v. Widmayer, 21 F.3d 1098, 1100-01 (Fed. Cir. 1994)*); see also *37 C.F.R § 1.601(j)*. n6 In order to determine whether the two parties claim the same patentable invention, the USPTO has promulgated a "two-way" test, which has been approved by this court. *Eli Lilly, 334 F.3d at 1270*. The two-way test reads as follows:

> Invention "A" is the same patentable invention as an invention "B" when invention "A" is the same as (*35 U.S.C. 102*) or is obvious (*35 U.S.C. 103*) in view of invention "B" assuming invention "B" is prior art with respect to invention "A". Invention "A" is a separate patentable invention with respect to invention "B" when invention "A" is new (*35 U.S.C. 102*) and non-obvious (*35 U.S.C. 103*) in view of invention "B" assuming **[*23]** invention "B" is prior art with respect to invention "A".

37 C.F.R. § 1.601(n). In order for an interference-in-fact to exist, invention A must anticipate or make obvious invention B, and invention B must anticipate or make obvious invention A, thereby meeting both prongs of the "two-way" test. *Eli Lilly, 334 F.3d at 1268*; accord *Winter v. Fujita, 53 U.S.P.Q.2d 1234, 1243* (Bd. Pat. App. & Int. Nov. 16, 1999). The Board in the present case worded the two-way test in a different way as follows:

> Thus, for Lederman to succeed in its motion for no interference-in-fact, Lederman need only demonstrate that: (i) Lederman's claims are not anticipated or rendered obvious by Noelle's remaining "mouse" claims; or (ii) Noelle's remaining "mouse" claims are not anticipated or rendered obvious by Lederman's claims.

(Emphasis in original).

Noelle's argument that the Board improperly required a two-way patentability test, or, as the Board phrased it, a "one-way distinctiveness" test, is without merit in light of this court's recent ruling in Eli Lilly upholding the Director's two-way test as consistent with **[*24]** the language of the regulation. *334 F.3d at 1268*. Therefore, the Board applied the proper "two-way test." First, it determined that "one skilled in the art lacked a reasonable expectation of success of obtaining Lederman's claimed 'human' subject matter when provided with Noelle's 'mouse' subject matter and using the screening techniques cited by Noelle." Although the Board did not have to conduct the second prong of the test to find no interference-in-fact, it did so anyway by finding that "one skilled in the art would have lacked a reasonable expectation of success of obtaining Noelle's 'mouse' subject matter when provided with Lederman's claimed 'human' subject matter and using the same screening methods." Therefore, the Board utilized the correct test to find no interference-in-fact.

Noelle's argument that the Board erred in its application of the obviousness question in the interference-in-fact analysis by ignoring the specification in Noelle's '480 application is also without merit. Both Lederman and Noelle concede that the anticipation portion of the interference-in-fact analysis is not an issue in light of the agreed variance between claims to mouse

versus human [*25] forms of CD40CR antibodies. Thus, only the obviousness analysis pursuant to *35 U.S.C. § 103* is left to be determined. Obviousness is determined as follows:

> a proper analysis under *§ 103* requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success.

In re Vaeck, 947 F.2d at 493. Both the suggestion and the reasonable expectation of success "must be founded in the prior art, not in the applicant's disclosure." Id.; see also *In re Dow Chem. Co., 837 F.2d 469, 473 (Fed. Cir. 1988)*.

The parties agree that a skilled artisan would have been motivated to obtain the human CD40CR antibody if the mouse CD40CR antibody were available. The two parties disagree, however, as to whether the prior art would provide a reasonable likelihood of success in so doing. Therefore, the issue before us is [*26] whether substantial evidence supports the Board's determination that one of ordinary skill in the art would not have had a reasonable expectation of success of isolating the other party's invention given the disclosures found in the claims. A reasonable likelihood of success does not necessarily mean an absolute predictability, but rather a reasonable expectation of success. *Yamanouchi Pharm. v. Danbury Pharmacal, Inc., 231 F.3d 1339, 1343 (Fed. Cir. 2000)*.

Noelle argues that the methods disclosed in his '799 patent application would have provided a reasonable likelihood of success for a person of ordinary skill in the art to isolate human CD40CR antibodies using mouse CD40CR antibodies. Specifically, Noelle argues it would have been obvious to a skilled artisan to use the CD40-Ig fusion protein disclosed in the '799 application as a screen to locate, within a hybridomal library, monoclonal antibodies that specifically bind to human CD40CR antigen. Noelle further argues the Board improperly ignored this method of antibody isolation merely because it was disclosed in Noelle's written description as opposed to Noelle's claims.

The Board correctly found no interference-in-fact [*27] between Noelle's claims and Lederman's claims. First, the Board was correct in not considering Noelle's methods of isolation of human CD40CR antigen using CD40-Ig found in his '799 specification because the methods were neither part of the parties' inventions nor "prior art." USPTO rules establish that an interference-in-fact exists when both parties claim the "same patentable invention." *37 C.F.R. § 1.601(n)*. A patentee's invention is only found in a patentee's claims, unless the patentee uses sufficient means-plus-function language to invoke *35 U.S.C. § 112*, paragraph (6). Thus, if the Board is to compare two inventions, the Board must only compare the parties' claims. Noelle does not claim a method of isolating CD40CR antigens, CD40-Ig, or the receptor CD40 itself. Obviously, if certain terms in Noelle's or Lederman's claims were ambiguous, we could resort to the specification or other sources to define those terms; however, it is unnecessary here as none of the terms in the claims are ambiguous. Therefore, Noelle cannot rely on a method of isolating human CD40CR antigen using CD40-Ig in order to prove obviousness between his invention [*28] and Lederman's invention because the method is not claimed.

Second, the Board's determination was supported by substantial evidence because a person of ordinary skill in the art, given the state of prior art at the time of the '799 filing, would not have had a reasonable likelihood of success in isolating human CD40CR antibodies from the mouse CD40CR antigen and its antibody. Noelle argues that one skilled in the art would have had a reasonable likelihood of success in manufacturing a set of hybridomas that secrete monoclonal antibodies to activated human helper T-cell surface antigens. Noelle, as outlined previously, cited three different screening methods disclosed in his specification that would isolate the desired hybridomas and their antibodies. The first two of Noelle's proposed screening methods require the use of CD40-Ig. As the expert testimony of Dr. Aruffo, the named inventor in the patent claiming CD40-Ig, indicated to the Board, it would have been unpredictable and unreasonable to expect a skilled artisan to produce CD40-Ig given the state of the art at the time.

Finally, Noelle's expert witness, Dr. Clark, addressed the third and final proposed screening method. Dr. [*29] Clark declared that, given the mouse form of CD40CR antibody or CD40-Ig and the utilization of expression cloning methods available at the time, a person of ordinary skill in the art would have had a reasonable expectation of success in isolating the human form of CD40CR antigen. Armitage, however, during the prosecution of his '703 application, stated that the use of expression cloning could not have reasonably led to successful isolation of human CD40CR antigen.

After examining the record as a whole, we conclude there was substantial evidence to support the Board's decision. The Board's decision was reasonable in that, given the state of the art in the early 1990s as described

by the expert witnesses, a person of ordinary skill in the art would not have had a reasonable likelihood of success in isolating human CD40CR antigen given mouse CD40CR antigen.

CONCLUSION

For the foregoing reasons, the decision of the Board rejecting claims 51, 52, 53, 56, 59, and 60 of Noelle's U.S. Application No. 08/742,480 is affirmed. The decision of the Board granting Lederman's preliminary motion of no interference-in-fact is also affirmed.

AFFIRMED

No costs.

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APPEAL NO. 02-1187

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

RANDOLPH J. NOELLE,

Appellant,

v.

SETH LEDERMAN, LEONARD CHESS, and MICHAEL J. YELLIN,

Appellees,

Appeal from the United States Patent and Trademark Office
Board of Patent Appeals and Interferences

BRIEF FOR APPELLANT RANDOLPH J. NOELLE

E. Anthony Figg
Glenn E. Karta
ROTHWELL, FIGG, ERNST & MANBECK
1425 K Street, N.W.; Suite 800
Washington, DC 20005
(202) 783-6040

Attorneys for RANDOLPH J. NOELLE

November 29, 2002

CERTIFICATE OF INTEREST

Counsel for Appellant Randolph J. Noelle certifies the following:

1. The full name of every party or amicus represented by me is: Randolph J. Noelle.

2. The name of the real parties in interest are: IDEC Pharmaceuticals Corporation and the Trustees of Dartmouth College.

3. The parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are: IDEC Pharmaceuticals Corporation.

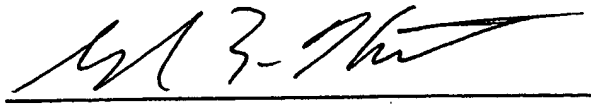
4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

E. Anthony Figg
Glenn E. Karta
ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K Street, NW, Suite 800
Washington, DC 20005
(202) 783-6040

Robin L. Teskin
PILLSBURY WINTHROP
1600 Tysons Boulevard
McLean, VA 22102
(703) 905-2000

R. Danny Huntington
BURNS, DOANE, SWECKER & MATHIS, L.L.P.
1737 King Street, Suite 500
Alexandria, VA 22314-2727
(703) 836-6620

Date: November 29, 2002



E. Anthony Figg
Glenn E. Karta
ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K Street, NW, Suite 800
Washington, DC 20005
(202) 783-6040

COUNSEL FOR APPELLANT
RANDOLPH J. NOELLE

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STATEMENT OF RELATED CASES

No other appeal in or from the same proceeding in the lower body was previously before this or any other appellate court.

STATEMENT OF JURISDICTION

A) The United States Patent and Trademark Office's jurisdiction below was based on 35 U.S.C. § 135(a).

B) The Court's appellate jurisdiction in this case is based on 28 U.S.C. § 1295(a)(4)(A) and 35 U.S.C. §§ 141 and 144, this being an appeal from an adverse decision of the United States Patent and Trademark Office Board of Patent Appeals and Interferences in an interference.

C) The final decision below was entered October 19, 2001. The Notice of Appeal was timely filed on December 19, 2001 pursuant to 35 U.S.C. § 142 and 37 C.F.R. § 1.301.

D) The present appeal is from a final decision in Interference No. 104,415.

STATEMENT OF THE ISSUES

1. Did the United States Patent and Trademark Office Board of Patent Appeals and Interferences err in denying Noelle benefit of the priority date of the '799 Application under 35 U.S.C. § 120 because of lack of written descriptive support under 35 U.S.C. § 112, paragraph one?

2. Did the United States Patent and Trademark Office Board of Patent Appeals and Interferences err in finding that Noelle's claims to a monoclonal antibody to human CD40CR were invalid under 35 U.S.C. §102(b)?

3. Did the United States Patent and Trademark Office Board of Patent Appeals and Interferences err in applying a two-way obviousness test to determine that no interference-in-fact existed between the Noelle application and the Lederman patent?

4. Did the United States Patent and Trademark Office Board of Patent Appeals and Interferences err in refusing to consider the teachings of Noelle's specification in its obviousness analysis in the context of determining the existence *vel non* of an interference-in-fact?

I. INTRODUCTION AND STATEMENT OF THE CASE

A. The Board's Decision

This is an appeal from a final decision of the United States Patent and Trademark Office Board of Patent Appeals and Interferences ("Board") in an interference between a patent application of Randolph J. Noelle ("Noelle") and a patent of Seth Lederman, Leonard Chess and Michael J. Yellin ("Lederman") . Lederman is senior party. The Board entered judgment for Lederman on two preliminary motions, the latter of which terminated the proceedings before the Board. Noelle seeks review of both decisions.

First, the Board determined that Noelle's involved claims that are generic to monoclonal antibodies ("MAbs") to the CD40CR surface antigen of both mouse and human T-lymphocytes (the "genus claims") and those that are specific to MAbs to the CD40CR surface antigen of human T-lymphocytes (the "human claims") are unpatentable under 35 U.S.C. § 102(b) over certain prior art that was published after the filing date of Noelle's grandparent application (February 14, 1992), but more than one year before the filing date of Noelle's parent application (November 14, 1994). JA 03824-JA03831; See also JA 00005-JA 00006. The parent application was a file wrapper continuation of the grandparent application,

but the Board had earlier ruled (JA 00064) that Noelle is not entitled to the benefit of the filing date of the grandparent, because the involved claims are not supported by an adequate written description in the specification of that application.

Noelle does not dispute that without the benefit of its grandparent application filing date, its involved genus and human claims are unpatentable over the intervening prior art. However, the Board erred in concluding that the genus claims lack adequate written description support under 35 U.S.C. §112 in the grandparent application. Therefore, the real issue before the Court is the written description issue. The Board departed from established precedent in concluding that Noelle's genus and human claims are unpatentable under §112, paragraph one, and it improperly applied the fact-specific holding of this Court in Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1562, 43 USPQ 2d 1398, 1401 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089 (1998) to the monoclonal antibody technology of this case.

Second, having concluded that Noelle's genus claims and human claims are unpatentable, the Board ruled that there was no interference-in-fact between the remaining involved claims of the Noelle application and the involved human claims of the Lederman patent. The Noelle claims are directed to MAbs to the CD40CR surface antigen of mouse T-lymphocytes (the "mouse claims") and the

Lederman human claims are directed to MAbs to the CD40CR surface antigen of human T-lymphocytes.

The Board erred in its decision on the interference-in-fact issue. Contrary to the plain meaning of applicable Patent and Trademark Office regulations, precedent of this Court and Board precedent, the Board applied a two-way obviousness test in determining whether the parties' respective claims were directed to the same patentable invention. As part of its two-way test for determining interference-in-fact, the Board also erroneously refused to consider the teachings of Noelle's specification in its obviousness analysis (determining reasonable likelihood of success).

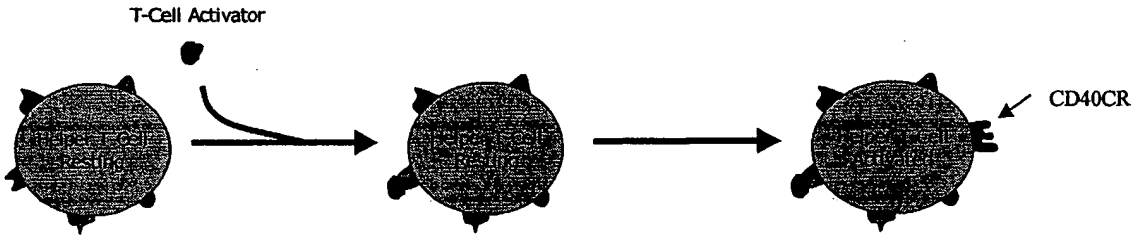
The finding of no interference-in-fact with respect to all of Noelle's remaining claims terminated the interference. Accordingly, the Board issued its Final Decision and entered final judgment on both of its decisions. (JA00001-JA00031).

B. Overview of the Technology

This interference involves MAbs that are useful for mediating reactions of the immune system. The parties' claims all are directed to MAbs to a membrane protein, known as CD40CR, that is expressed on the surface of activated, but not

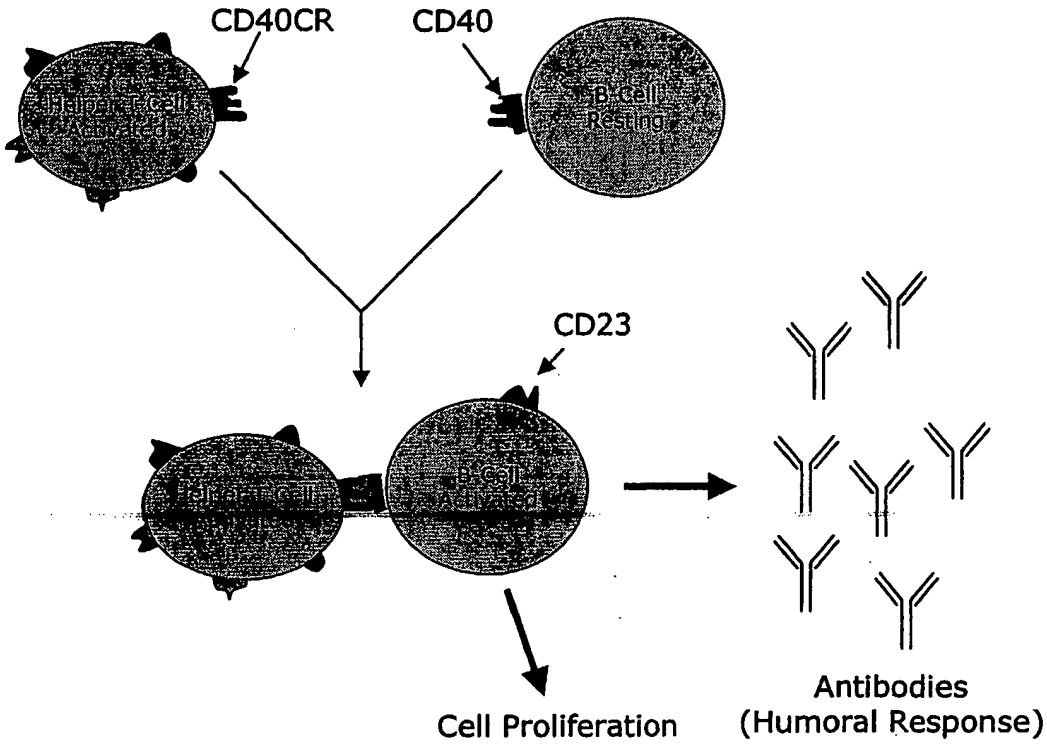
resting, T-lymphocytes or T-cells[1]. CD40CR is the ligand for a membrane receptor, CD40, of B-lymphocytes (B-cells). When T-cells are activated, they express the CD40CR protein. CD40CR, in turn, binds to its receptor, CD40, on B-cells and that binding, together with other factors, results in the activation of B-cells. Activation of B-cells results in B-cell proliferation and antibody production (a humoral response). At an oral hearing before the Board, both parties used the following visual aids to illustrate the cellular processes. (See JA 00259 and 00260):

Activation of T-Cells and Expression of CD40CR



[1] CD40CR is also known as CD40 ligand, CD40L, CD40 counter receptor, gp39 and 5c8 antigen JA 00041 at ¶ 11. For consistency, it will be referred herein as CD40CR.

T-Cell Contact Activation of B-Cells



MAbs described in the parties' specifications bind to the CD40CR surface protein and block the sites at which it binds to CD40, thereby inhibiting T-cell contact activation of B-cells. MAbs having this activity are useful for mediating immune reactions and for treating allergies, autoimmune disorders and the like.

C. Summary of Issues on Appeal

1. Written Description

The Board's opinion and order on the written description issue are set forth in Paper No. 108 (JA 00032-JA 00076). Relying principally on this Court's decision in Regents of Univ. of Cal. v. Eli Lilly & Co., the Board concluded that, because Noelle had not, as of the filing date of the grandparent application, actually produced a MAb to the CD40CR of human T-cells, and Noelle described such MAb by its binding specificity rather than its structure, the human claims and the genus claims of Noelle's application were not described in that application in compliance with §112, paragraph one.

The Board correctly determined that a principal purpose of the written description requirement is to ensure that the applicant possessed the claimed invention as of the applicable filing date, citing Vas Cath v. Mahurkar, 935, F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). However, the Board erroneously confused possession of the invention with possession of physical materials resulting from an actual reduction to practice. The latter is not required for compliance with §112, paragraph one, which requires only that the invention be adequately described.

While acknowledging that the written description analysis is highly fact laden, the Board ignored the substantial differences between the DNA subject matter of Regents of Univ. of Cal. v. Eli Lilly & Co. and the MAb technology of this case. Antibodies have long been described by their binding specificities, and not by their amino acid sequences, their chemical formulas, their molecular weights or other physical or chemical characteristics. Antibodies are well-characterized biomolecules whose overall structure was known to scientists skilled in immunology in 1992. Unlike the DNA molecules at issue in Regents of Univ. of Cal. v. Eli Lilly & Co. (whose nucleotide sequences often must be known to describe them adequately), the sequence of an antibody rarely is known and need not be known either to describe it or to enable its preparation and use. Antibodies are made by immunization of an animal. Specificity to the antigens in the immunogen is achieved by the animal's immune system. Neither the structure of the immunogen, nor that of the resulting antibodies need be known. JA02580-JA 02586. For this reason, scientists conventionally describe antibodies by their binding specificity (*e.g., see*, In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) (antibody to hepatitis B surface antigen).

The Board erred by focusing on the lack of structural or sequence information for the CD40CR immunogen and the claimed MAbs. Neither party's

specification contained such information, yet both parties obtained MAbs to CD40CR using very similar procedures.

2. Interference-In-Fact

The Board's opinion on the interference-in-fact issue is in Paper No. 135 (JA 00001-JA 00031). The Board erred in two principal ways concluding that Noelle's and Lederman's claims do not interfere. First, the Board applied a two-way obviousness test. The Board mischaracterized its test as a one-way distinctiveness test; however, it concluded that Lederman could succeed in its motion by demonstrating either (1) that Lederman's claims are not anticipated by or obvious over Noelle's claims, or (2) that Noelle's claims are not anticipated by or obvious over Lederman's claims. In other words, under the Board's test, an interference exists only if the parties' respective claims are the same as (35 U.S.C. §102) or obvious (35 U.S.C. §103) in view of each other in both directions. This test is illogical and contrary to the applicable regulations (37 C.F.R. §1.601(j) and (n)) and precedent of this Court and the Board. The test also is contrary to public policy, because it will lead to the issuance of two patents to different entities that claim the same invention.[2] The Board should have required Lederman, as the

[2] For example, it allows patents to a later-invented genus and an earlier-invented species to issue to different entities.

moving party, to prove that the invention defined by its involved claims was patentable over the invention defined by Noelle's claims, assuming the latter to be prior art to Lederman.

Second, as part of its two-way obviousness test, the Board also refused to consider the teachings of the Noelle specification. Without citation of any authority, the Board concluded that, "the parties' specifications.... are not available as 'prior art' for determining whether an interference-in-fact exists." JA 00018. As a result of this conclusion, the Board refused to consider the teachings of the Noelle specification with respect to how to obtain the claimed MAbs. This information therefore was not considered by the Board in its analysis of the "reasonable expectation of success" prong of the obviousness analysis. The Board considered only the prior art (published literature) existing prior to the parties' filing dates.

The Board erred in refusing to consider the teachings of the Noelle specification. The applicable rules require comparison of the parties' inventions. See 37 C.F.R. §1.601(j) (interference-in-fact exists if parties respective claims "define the same patentable invention.") and § 1.601(n) ("Invention 'A' is the same patentable invention as an invention 'B' when invention 'A' is the same as (35 U.S.C. §102) or is obvious (U.S.C. §103) in view of invention 'B' assuming

invention 'B' is prior art with respect to invention 'A'."). When, as here, the claimed invention is a novel composition of matter, the subject matter in the specification that teaches how to obtain that composition of matter must be considered in determining whether the moving party's claimed invention is obvious over the invention claimed by the non-moving party, *e.g.*, determining whether a person of ordinary skill in possession of the other party's invention would have had a reasonable likelihood of success of obtaining the claimed composition of matter. The Board's refusal to consider the teachings of the specification can lead to absurd results. For example, under the Board's approach, using the language of Rule 1.601(n), if B claimed a novel composition of matter and described how to make it in the specification, a patent nevertheless would issue to A for a claim to a patentably indistinct related composition of matter assuming that the prior art published before B's filing date did not teach how to obtain the composition of matter (as is usually the case for novel compositions). Without the teachings of B's specification, B would be unable to establish that skilled persons would have had a reasonable expectation of success. A's claims, however, would be invalid under 35 U.S.C. §102(g), because the teachings of B's (assumed here to be the prior inventor) specification would be available as prior art in a §102(g) challenge to A's patent. Thus, the very issue that the Board is

required to resolve --conflicts under §102(g)-- is sidestepped under the Board's approach and are left for later resolution in a federal court. Because the rules require comparison of the parties' respective inventions for patentable distinctness, there is no logical reason for ignoring those aspects of the written description that teach how to obtain that invention.

The evidence of record shows that, had the Board applied the proper test, Lederman's claimed invention (MAbs to human CD40CR) would have been found obvious over Noelle's claimed invention (MAbs to mouse CD40CR).

II. STATEMENT OF FACTS

A. The Patent and Patent Applications Involved in the Interference

1. Lederman United States Patent 5,474,771 (the "'771 Patent")

The '771 patent resulted from Application No. 792,728, filed on November 15, 1991. The application describes and claims a monoclonal antibody to "the 5c8 antigen located on the surface of activated T cells and thereby inhibits T cell activation of B cells." JA 00303, col. 31, lines 6-8, Claim 1. The monoclonal antibody 5c8 is Lederman's designation of an antibody that binds to CD40CR expressed on the surface of activated human T-cells. JA 00298 at col. 22, lines 34-57. The '771 patent claims the murine, chimeric, humanized and human forms of the monoclonal antibody. JA 00303, Claims 4-7.

2. The Noelle Applications

The Noelle application involved in the interference, Serial No. 08/742,480 (the "'480 application"), discloses and claims monoclonal antibodies to CD40CR, just as does the '771 patent. The '480 application is a continuation of Serial No. 08/338,975 (the "'975 application") filed on November 14, 1994 which, in turn, is a continuation of Serial No. 07/835,799 (the "'799 application"), filed on February 14, 1992. The 1992 application contained working examples describing the preparation of a MAb (designated "MR1") to CD40CR expressed on the surface of activated mouse T-cells. JA 00332, sec. 6.1.12. The Noelle application discloses that CD40CR is expressed generally on the surface of activated T-cells and specifically on human T-cells. JA00324 at lines 5-8; JA00336 at sec.6.2.3; and JA00339 at sec.7. It describes a soluble fusion protein, designated CD40-Ig, which is a fusion of the human B-cell CD40 receptor (*i.e.*, the natural receptor for human CD40CR) and the constant region of an immunoglobulin. JA 00330-JA 00331 at section 6.1.7. It describes the use of this fusion protein for the characterization and purification of CD40CR (JA 00336 at Section 6.2.3) and it describes its binding to human T-cell lines. JA 00339 at section 7.

The Noelle application describes the purification of CD40CR from human T-cell lines using a combination of standard protein purification procedures,

followed by affinity chromatography using, for example, the human CD40-Ig fusion protein. JA 00324 at section 5.3. The application also describes the preparation of MAbs to CD40CR using, *inter alia*, known hybridoma technology. JA 00319-JA 321 at section 5.1.2; JA 00332 at section 6.1.12. It explains that immunogens (substances used to immunize animals) that may be employed for the preparation of MAbs include activated T-cells and purified CD40CR prepared as described in Section 5.3 (*i.e.*, including purified human CD40CR).

The specification of the Noelle application describes a number of uses for ligands that bind CD40CR. JA 00325 at section 5.4. Such ligands include the claimed MAbs. JA 00316-JA 00321 at section 5.1; JA 00336-337 at section 6.2. The disclosed uses for such MAbs include the treatment of a wide variety of human disorders that are associated with B-cell activation. JA 00325-JA 329.

Noelle's application clearly describes MAbs to human CD40CR. It describes that human CD40CR is present on activated human T-cells and T-cell lines, and substantiates the description with experimental data showing that the natural human receptor, CD40, binds to activated human T-cell lines. JA 00339 at section 7. It describes how to use activated human T-cells and T-cell lines to make the MAbs. JA 00319-JA 00321 at section 5.1.2; JA 00332 at section 6.1.12. It describes screening methods for identifying MAbs that bind specifically to

CD40CR. JA 00332 at sections 6.1.12 (selective recognition of activated T-cells) and JA 00336-JA 00337 at 6.2.4 (inhibition of contact mediated activation of B-cells by plasma membranes of activated T-cells).

Thus, Noelle described the invention claimed in the genus claims and the human claims, *i.e.*, MAbs that bind generally to CD40CR and specifically to human CD40CR.[3] Noelle's description of the MAbs by reference to their binding specificity rather than by amino acid sequence or structure, was consistent with decades of custom and practice in the field of immunology. See Section IV.B.3., infra.

B. The Level of Ordinary Skill and the Pertinent Teachings of the Prior Art

As of the filing date of the Lederman patent, the level of ordinary skill in the pertinent field of science was high. JA 00047-JA 00048. As of November 15, 1991, one skilled in the preparation of monoclonal antibodies had many available and reliable research tools at his or her disposal, as well as extensive experience.

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[3] Much of the Board's opinion and much of the argument presented by Lederman dealt with conflicting expert opinions about whether the techniques that Noelle described for making anti-CD40CR MAbs would work (or would have been expected to work) for the preparation of MAbs to human CD40CR. However, as discussed below in Section IV(B)(2), those arguments relate to the issue of enablement, which is not before the Court and which is separate and distinct from the issue of written description.

Skilled scientists would have known that both mouse and human B cells express CD40, one of the antigens involved in B cell differentiation. JA 01487, last paragraph. It was also known that mouse activated T-cells and T-cell lines expressed a cell surface structure that induced T-cell contact-dependent B-cell activation. JA 03214; JA 03226.

Human T-cells and T-cell lines were known which expressed surface structure involved in B-cell activation. JA 00142-JA 00149. Indeed, this fact was publicly disclosed by the inventors of the '771 patent before either party's filing date. JA 00150-JP 00152. Upon the addition of lymphokines, fixed activated human T-cells or T-cell lines were known to induce B-cell cycle entry followed by B-cell proliferation and differentiation. JA 00153-JA 00161. Certain important surface molecules known to be necessary for B-cell activation were known to be expressed on activated T-cells, but not resting T cells. Id.

The parties did not dispute that methods for obtaining and screening monoclonal antibodies were well known prior to November 15, 1991, and, in fact, were in use as early as 1980. Ex parte Erlich, 22 USPQ2d 1463, 1466 (Bd. Pat. App. & Int. 1992). Along with the basic methods for screening and testing the monoclonal antibodies, skilled scientists were familiar with the requirements for generating immune responses, including humoral and cellular responses, the cell

types and interactions between the cells involved in the establishment of cell responses, and the molecules which were responsible for these interactions. JA 00566 at ¶ 10; JA 00534 at ¶ 8. The factors which augmented or suppressed immune responses also were known. Id. Most importantly, methods for generating monoclonal antibodies which specifically bound protein antigens -- including antibodies which modify immune response -- were known. Id.

Techniques for producing monoclonal antibodies to an uncharacterized antigen with a specific known function also were available. JA 02580-JA 02587. The most commonly used technique to accomplish this task was screening for antibodies that block the known function of the antigen. Id. In fact, this was the method used by both Noelle and Lederman. JA 00337 at lines 23-31; JA 00298 at col. 22, lines 20-29. It was routine to use a functional screen to identify MAbs that inhibit T-cell activation of B-cells. JA 02886 at ¶¶ 33-34.

Both parties' experts agreed that activated T-cells (human or mouse) or membranes from those cells could be used as immunogens. For example, Noelle's expert, Dr. Clark, testified that it "would reasonably have been expected that the immunization of an appropriate host with activated T cells, membranes derived therefrom, or CD40CR expressing T cell lines would have elicited antibodies

specific to CD40CR." JA 03516 at ¶ 32. Lederman's expert, Dr. Shevach, acknowledged that he had routinely used immune cells as immunogens and had used this technique for making antibodies against T-cell antigens. Similarly, he acknowledged that it was known to produce antibodies against cell membrane extracts. JA 02580-JA 02581. There is no dispute that methods of activating T-cells using substances such as anti-CD3 or PMA were known. JA 00247.

It also was undisputed that knowledge of the DNA sequence of the gene encoding the antigen to which the antibody binds was unnecessary to make antibodies to that antigen. JA 02586; JA 02616; JA 02726. Moreover, the sequence is not necessary for sufficient characterization of the antigen or the antibody. JA 02586. An antibody is adequately characterized functionally by identifying an antigen to which the antibody binds. JA 02587.

C. The Noelle Specification Describes the Preparation of MAbs to Human CD40CR

The Noelle application describes the preparation of MR1, a MAb that binds specifically to CD40CR expressed on activated mouse T-cells. JA 00332-JA 00337. MR1 and the human CD40-Ig fusion protein bound to a single antigen on the surface of active but not resting mouse T-cells. JA 00336; JA00351. This antigen, CD40CR, had a molecular weight of 39kD. JA 00336-JA00337;

JA00351. The Noelle specification describes experiments showing that MR1 and the human CD40-Ig fusion protein (but not other antibodies) inhibit T-cell activation of B-cells. JA 00337. Thus Noelle established the existence of CD40CR and characterized it as the ligand for the B-cell receptor, CD40.

It was known that both human and mouse B-cells expressed the CD40 surface antigen. JA 01487, last ¶. In proceedings before the Board, the parties did not dispute that skilled artisans would have expected that an antigen expressed on the surface of mouse T-cells would have a homolog or counterpart on human T-cells. See JA 02874 at ¶ 18: ("[I]t would have been unexpected had CD40CR not been expressed on human T cells, given the fact that human and mouse T cells and membranes therefrom were known to respectively interact with human or mouse B cells [in] similar contact-dependent manner and elicit B cell activation and differentiation."); JA 02638-JA02640: ("[B]etween mouse and human, most surface molecules are conserved, have a strong relationship."). This conservation across species explains why immunologists use mouse systems as a model to study human immune functions. JA 02632-JA 02633. Indeed, in proceedings before the Board, Lederman presented no evidence of any T-cell antigen that existed in mouse but not humans, or vice versa.

Accordingly, Noelle possessed the invention of a human CD40CR and its use to prepare MAbs to human CD40CR as of his 1992 filing date. He thus possessed the invention of his genus claims and his human claims as of his filing date, and he fully described the invention in his patent specification in detail that was scientifically customary for the description of MAbs.

As of February 14, 1992, it was known that human and mouse CD40 were functionally analogous based on evidence that the two proteins displayed similar tissue distribution, similar patterns of expression in cell lines, increased level of expression of RNA and protein in activated B-cells when induced by the same agents, and conservation of aligned cysteine residues in the extracellular domain which suggested similar tertiary structure and folding. JA 02998-JA 3004. For antigens expressed on T-cells or B-cells involved in immune function and regulation, the overwhelming majority of identified antigens exhibit significant conservation of structure. JA 02874 at ¶ 18.

The Noelle specification teaches one of skill in the art that MR1 and human CD40-Ig bind the same CD40CR antigen expressed on mouse T cells. JA 02649-JA 02650. Because CD40-Ig contains the human receptor, a person of skill in the art would have expected human CD40-Ig to bind to human CD40CR with at least as much affinity as to mouse CD40CR. JA 02737, JA 02738 and JA 02759.

D. Interference No. 140,415 - Procedural History

Interference No. 104,415 was declared on September 3, 1999, with Count 1 which reads as follows:

> The monoclonal antibody of claim 1 of 5,474,771 [Lederman] or the monoclonal antibody of claim 42 or claim 51 of 08/742,480 Noelle].

JA 00005, Interference paper No. 135 at n.1. See also, JA 00038-JA 00039, ¶¶ 5-7. The Board found that the above count contains three different embodiments, including: the murine CD40CR monoclonal antibody, the human CD40CR monoclonal antibody and the CD40CR monoclonal antibody as a genus. JA 00005.

The Board determined that Noelle's genus claims and human claims were not entitled to the filing date of the 1992 grandparent application based on what it ruled to be a deficient written description. JA 00062. Thus, Noelle was not accorded the February 14, 1992 priority date and was granted the November 14, 1994 priority date under the '975 application. JA 00065. As a result, Noelle's genus claims and human claims were rejected under 35 U.S.C. § 102(b) based on two intervening prior art references. JA 00006; JA 03824-JA03831.

Finding Noelle's genus claims and human claims to be unpatentable, the Board determined that the issue of interference-in-fact was ripe for consideration

and ordered the parties to submit briefs regarding that issue. After Oral Argument on the interference-in-fact issue, the Board issued its Final Decision on October 19, 2001, holding that no interference-in-fact existed. JA 00001-JA 00031.

III. SUMMARY OF THE ARGUMENT

The Board erred in concluding that Noelle's genus claims lacked adequate written description support under 35 U.S.C. § 112, paragraph one, in Noelle's grandparent application filed February 14, 1992. Consequently, the Board's holding that Noelle's genus claims were unpatentable under 35 U.S.C. § 102(b) over prior art published after February 14, 1992 should be reversed.

The Board also erred in concluding that there was no interference-in-fact between Noelle's mouse claims and Lederman's human claims. In particular, it was error (i) to apply a two-way obviousness test, rather than the one-way test mandated by the Patent and Trademark Office rules and Court and Board precedent; and (ii) to refuse to consider the teachings of Noelle's specification on the issue of reasonable likelihood of success.

IV. ARGUMENT

A. Standard of Review

Although the determination of whether a prior application meets the requirements of 35 U.S.C. § 120 is a matter of law, the determination underlying the issue - whether the specification of the priority application sufficiently describes the newly claimed invention under 35 U.S.C. § 112 - is a question of fact. Ralston Purina Co. v. Far-Mar-Co., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985); Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Likewise, although the determination of obviousness (as part of the interference-in-fact analysis) is a matter of law, the Board determined underlying factual issues in support of that determination. Richardson-Vicks, Inc. v. Upjohn Co., 122 F.3d 1476, 1479, 44 USPQ2d 1181, 1183 (Fed. Cir. 1997). However, the Board's decision on the interference-in-fact issue was based on an error of law -- the application of improper tests for determining whether the claims of the Noelle application and those of the Lederman patent define the same patentable invention. See Section I(C)(2), infra. The determination of whether claims are unpatentable based on anticipation under 35 U.S.C. § 102 is a question of fact. Telemac Cellular Corp. v. Topp Telecom, Inc., 247 F.3d 1316, 1327, 58 USPQ2d 1545, 1552 (Fed. Cir. 2001).

The Board's legal determinations and conclusions are reviewed *de novo*. In re Gartside, 203 F.3d 1305, 1316, 53 USPQ2d 1769, 1776 (Fed. Cir. 2000). This Court reviews the Board's factual findings under the substantial evidence standard. Id., 203 F.3d at 1315, 53 USPQ2d at 1775. To apply a substantial evidence standard, this Court must "examin[e] the record as a whole, taking into account evidence that both justifies and detracts from an agency's decision." Id. at 1312, 53 USPQ2d at 1773 (citing Universal Camera Corp. v. NLRB, 340 U.S. 474, 487-488 (1951)).

B. Noelle Should Have Been Granted the Priority Date of the '799 application Under 35 U.S.C. § 120

1. Qualifying for Priority Under 35 U.S.C. § 120 and Written Description Under 35 U.S.C. § 112 ¶ 1 - The Legal Requirements

To qualify for priority under 35 U.S.C. § 120, "the disclosure of the application as originally filed [must] reasonably convey [] to the artisan that [the inventor] had possession at that time of the later claimed [invention]." Utter v. Hiraga, 845 F.2d 993, 999, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988) (quoting In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). To meet this test, there is no requirement that the specification contain what is known in the art. Martin v. Mayer, 823 F.2d 500, 504-505, 3 USPQ2d 1333, 1337 (Fed. Cir. 1987).

Moreover, because the determination of these types of questions are so intensely fact specific, "each case much be decided on its own facts. Thus, the precedential value of cases in this area is extremely limited." Vas-Cath, Inc., 935 F.2d at 1562, 19 USPQ2d at 1116 (quoting In re Application of Driscoll, 562 F.2d 1245, 1250, 195 USPQ 434, 438 (CCPA 1977). See also, In re Edwards, 568 F.2d 1349, 1354, 196 USPQ 465, 469 (CCPA 1978).

The manner in which the written description requirement is met is not important, only that it is met as between the prior application's specification and the present application's claims. Edwards, 568 F.2d at 1352, 196 USPQ at 467. "[O]ur primary concern is whether the description requirement has been complied with, not the mode selected for compliance." Id.

2. The Board Confused the Written Description and Enablement Requirements

An underpinning of the Board's decision on the written description issue was its conclusion that the relevant art was unpredictable as of Noelle's February 1992 filing date. In reaching this conclusion, the Board confused the requirements for written description and enablement. This Court has laid to rest the question of whether those two concepts are interrelated. Vas-Cath, Inc., 935 F.2d at 1563, 19 USPQ2d at 1117 ("[W]e hereby reaffirm, that 35 U.S.C. § 112, first paragraph,

requires a 'written description of the invention' which is separate and distinct from the enablement requirement.").

> In concluding that the art was unpredictable, the Board focused on whether the skilled artisan could have predicted with any reasonable degree of certainty from Noelle's disclosure whether particular CD40CRs and the antibodies specific to the CD40CRs could be generated and isolated other than Noelle's mouse CD40CR and the antibodies specific to mouse CD40CR.

JA 00048. Thus, in assessing whether there was an adequate written description of the claimed compositions of matter (the monoclonal antibodies), the Board improperly focused its attention on the methods used for making them. The Board questioned whether the procedures disclosed in Noelle's specification would work – an enablement question. In re Wands, 858 F.2d at 740, 8 USPQ2d at 1406-1407. There can be no dispute that Noelle described MAbs to human and mouse CD40CR, disclosed the source of human and mouse CD40CR (activated T-cells), disclosed procedures for making and identifying MAbs to mouse and human CD40CR, disclosed that human CD40-Ig fusion protein bound to human T-cells, and described the use of anti-human CD40CR MAbs for human therapeutic applications. See Sections A and B, supra. Whether the procedures disclosed by

Noelle work is an enablement issue that was not decided by the Board and is not before this Court.[4]

At Lederman's urging, the Board focused on the absence of sequence or structural information concerning CD40CR antigens from human and other species. JA 00049. However, the claims are not directed to CD40CR, they are directed to MAbs to CD40CR. The experts for both parties agreed that sequence or structural information for CD40CR was not necessary to make MAbs to it. See Section II(B), supra. Noelle successfully prepared a MAb to mouse CD40CR and Lederman successfully prepared a MAb to human CD40CR and neither of them possessed sequence or structural information for the CD40CR.

Significantly, the Board did not conclude that it was unknown or unpredictable that human CD40CR existed or had a different function than mouse CD40CR. Both parties' experts agreed that the human homolog of mouse CD40CR would have been expected to exist. See Section II, B and C, supra. It also was known that the receptor for CD40CR was expressed on both human and

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[4] Enablement is an objective test. In re Wright, 999 F.2d 1557, 1561, 27 USPQ 2d 2510, 1513, (Fed. Cir. 1993). A party challenging whether procedures described in a specification work as described normally must present evidence (such as experimental evidence) that they do not work. Similarly, the patent applicant may present evidence (including post-filing evidence) showing objectively that the teachings are enabling.

mouse B-cells. No substantial evidence supports a conclusion that it was unpredictable as to whether or not Noelle's experimental findings in the mouse model (i.e., the existence of CD40CR on activated T-cells and its role in contact mediated activation of B-cells) were applicable to the human immune system. Indeed, the evidence is to the contrary. Whether those findings and procedures actually work is an issue for another day.

In the same vein, the Board devoted considerable attention to the issue of whether the experimental results in Section 7 of Noelle's specification were valid. JA 00050. Lederman's experts criticized the results, because Section 7 of Noelle's application did not refer to a control experiment to prove that the binding of the human CD40-Ig fusion protein to human T-cells was through CD40CR-CD40 interaction, rather than through non-specific binding or binding through the immunoglobulin portion of the molecule. Id. Again, this is an enablement, not a description issue. Noelle referred to the work as confirmatory evidence that the tested T-cell lines possessed the CD40CR antigen, which further evidences Noelle's description of MAbs to human CD40CR. Lederman's experts' speculations that the experiment might not have demonstrated what it purported to

demonstrate (a fact that is contested by Noelle and which Lederman did not even try to prove) is at best an enablement, not a description, issue.[5]

3. Monoclonal Antibodies Are Described by their Binding Specificities, as in Both the Noelle Application and the Lederman Patent

In Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d at 1568, 43 USPQ2d at 1406 and Fiers v. Revel, 984 F.2d 1164, 1169, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993) this Court addressed situations in which the patentee (or applicant) sought claims that encompassed novel DNA molecules that, as of the filing date, could not be described in terms of structure, formula, chemical name or physical properties. Instead, the claims and the supporting description defined the DNA molecules by reference to their function (coding for the proteins of interest) and general methods for their synthesis. The Court held that such descriptions of DNA molecules were inadequate for compliance with the written description requirement of §112, ¶ 1. Eli Lilly & Co., 119 F.3d at 1568, 43 USPQ2d at 1406; Fiers, 984 F.2d at 1169, 25 USPQ2d at 1605.

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[5]The Board's reference to Dr. Aruffo's declaration showing that making the human CD40-Ig fusion protein prior to Noelle's 1992 patent application could not be predicted and also is a red herring. Noelle describes how to make the fusion protein (JA 00330 at Section 6.1.7); therefore, whether or not it was difficult or unpredictable to make human CD40-Ig before Noelle's filing date is irrelevant to the written description issue.

The Board's heavy reliance on Eli Lilly & Co. in this case is misplaced. The facts of Eli Lilly & Co. are quite different from those of this case. While the nucleotide sequence of a DNA molecule often is essential to show that the patent applicant possessed the invention, the same is not true of the amino acid sequence of a monoclonal antibody. Sequence data is routinely presented in patents claiming DNA molecules and other nucleic acids (see 37 C.F.R. 1.821), but rarely is such information included to describe antibodies.[6] Antibodies are (and were in 1992) well-defined biomolecules. They are produced by an animal's immune system upon immunization with an appropriate immunogen. In this case, Noelle identifies activated T-cells and isolated CD40CR as appropriate immunogens. See Section II, supra. It is the animal's immune system that determines the specificity of an antibody.

Extension of the rationale of Eli Lilly & Co. and Fiers to patent claims directed to MAbs would be unjustified and scientifically untenable. Scientists wishing to obtain patent protection on novel MAb's would be required to

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[6]See, e.g., Ex parte Erlich, 22 USPQ2d 1463 (Bd. Pat. App & Int. 1992); Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 2000); and Staehelin v. Secher, 24 USPQ2d 1513 (Bd. Pat. App. & Int. 1992). Each of these cases involved claims to antibodies or their uses in which the antibodies were defined by their binding specificities. In none of them were the involved antibodies defined by sequence or structure.

determine their amino acid sequences–information often having little or no scientific value to them.

The practice in the United States Patent and Trademark Office and the precedent of this Court confirm that antibodies typically are described by their binding specificities. Enzo Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002), (citing Synopsis of Application of Written Description Guidelines, at 60, available at http://www.uspto.gov/web/patents/guides.htm). This type of description meets the requirements of 35 U.S.C. § 112 ¶1 because the determination is made from the viewpoint of one of skill in the art at the time of the initial application. Reiffin v. Microsoft Corp., 214 F.3d 1342, 1346, 54 USPQ2d 1915, 1917-18 (Fed. Cir. 2000).

These long-established practices were ignored in this case. In the '799 application, the written description supported claims to the human antibody and the murine antibody as well as to the genus of antibodies which specifically bind to CD40CR.

Functional descriptions of inventions are adequate for § 112, paragraph one, written description compliance, provided that they would convey to a skilled artisan what was invented. In re Hayes Microcomputer Prods. Patent Litig., 982

F.2d 1527, 1534, 25 USPQ2d 1241, 1246 (Fed. Cir. 1992) (holding that disclosing a microprocessor capable of performing certain functions is sufficient to satisfy the requirement of § 112, first paragraph, when one skilled in the relevant art would understand what is intended and know how to carry it out). An applicant's disclosure obligation varies according to the art to which the invention pertains. Id.

Antibodies are typically described by their binding specificity. Staehelin v. Secher, 24 USPQ2d 1513, 1520 (Bd. Pat. App. & Int. 1992) (Board holding that the description of a monoclonal antibody "capable of specifically binding to at least one antigenic determinant of interferon-alpha" was sufficient for § 112, paragraph one, compliance. See also Kate H. Murashige, "Genome Research and Traditional Intellectual Property Protection–A Bad Fit," 7 Risks: Health, Safety and Environment 231, 234 (1996) (stating that Patent and Trademark Office Practice is to grant protection for antibodies claimed in functional terms).[7]

This Court has held, in the context of determining whether a conception of a biotechnological invention was complete, that the inventor need not have actually

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[7]Also see Janice M. Mueller, "The Evolving Application of the Written Description Required to Biotechnological Inventions," 13 Berkeley Tech. L.J. 615 (1998) (cautioning against extending the rationale of Eli Lilly & Co. to other types of biotechnological inventions).

reduced the invention to practice or even have had a basis for believing that it would work in order adequately to describe it. Burroughs Wellcome Co. v. Barr Labs., 40 F.3d 1223, 1231, 32 USPQ2d 1915, 1921-1922 (Fed. Cir. 1994), cert. denied, 515 U.S. 1130 (1995). Here, the Board confused possession of the invention–required for § 112, paragraph one, compliance–with physical possession of a MAb to human CD40CR. The latter, which would be the result of an actual reduction to practice, is not required for a sufficient written description.

In its recent decision in Enzo Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d at 1324, 63 USPQ3d at 1613 (Fed. Cir. 2002), this Court distinguished a functional description of DNA molecules (defined only by their ability to bind selectively to genomic DNA of a bacterium) from a functional description of an antibody. The Court observed that the Patent and Trademark Office's Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶ 1 Written Description Requirement, 66 Fed. Reg. 1099, 1110 n. 42 (June 5, 2001), permit a description in terms of "functional characteristics when coupled with a known or disclosed correlation between function and structure." Id. It referred to the "Synopsis of Application of Written Description Guidelines" for its conclusion that a claim to "[a]n isolated antibody capable of binding to antigen X" is sufficient for § 112, paragraph one, compliance considering "the well defined

structural characteristics of the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature." Id.

In Enzo Biochem, the Court found that these factors did not apply to the claimed DNA molecules. However, they are directly applicable here.

The Board erred in concluding that Noelle's human and genus claims are not supported by an adequate written description. The Board confused the description and enablement requirements and improperly extended the fact-specific holdings in Eli Lilly & Co. and Fiers to the substantially different facts and technology of this case.

C. Had Noelle Been Granted the Priority Date of the '799 Application Under 35 U.S.C. § 120, the Rejections Based on Anticipation Would Have Been Obviated

Had Noelle been given 35 U.S.C. § 120 benefit of the '799 application, the date of his constructive reduction to practice would have been set at February 14, 1992. Hyatt v. Boone, 146 F.3d 1348, 1350, 47 USPQ2d 1128, 1129 (Fed. Cir. 1998), cert. denied, 525 U.S. 1141 (1999). As a result of the Board's June 29, 2002 decision, the earliest filing date accorded to Noelle under 35 U.S.C. § 120 was the filing date of the '975 application, November 14, 1994.

The Board, in the June 29, 2001 decision, stated that because Noelle lacked the benefit of the earlier date, many intervening references rendered Noelle's genus and human claims unpatentable under 35 U.S.C. § 102(b). Specifically, the Board held that "[a] review of the record indicates that there are numerous publications and references that, while not available as prior art against Noelle's '799 February 14, 1992 filing date, are available under 35 U.S.C. § 102(b) against Noelle's '975 filing date of November 14, 1994." (Paper 109) JA 03823; See also JA 00005-JA 00006. ("Lacking the benefit of its 1992 filing date, [. . .] the Judge issued an Order under 37 C.F.R. § 1.641 rejecting Noelle's "genus" and "human" claims as anticipated by the disclosures of [two prior art references]") . These interceding references would not have been prior art had Noelle been granted his February 14, 1992 priority date.

Because the Board erred in its written description decision, claims filed in the '480 application are entitled to the benefit of the '799 application's February 14, 1992 filing date. Therefore, the references cited in Paper 109 do not qualify as prior art to the claims of the '480 application.

D. Because Noelle Should Have Been Granted Priority from the '799 Application, Noelle must Be Given the Opportunity to Present His Case Regarding Actual Reduction to Practice Prior to November 15, 1991

As a result of Noelle's entitlement to the priority date of February 14, 1992 as his constructive reduction to practice, Noelle may challenge the Lederman constructive reduction-to-practice date of November 15, 1991 by proving an actual reduction to practice at an earlier date. Cooper v. Goldfarb, 154 F.3d 1321, 47 USPQ2d 1896 (Fed. Cir. 1998).

The applicable statute reads, in pertinent part:

> Whenever an application is made for a patent which, in the opinion of the Commissioner, would interfere with any pending application, or with any unexpired patent, an interference may be declared and the Commissioner shall give notice of such declaration to the applicants, or the applicant and patentee, as the case may be. The Board of Patent Appeals and Interferences *shall determine questions of priority* of the inventions and may determine questions of patentability.

35 U.S.C. § 135(a) (emphasis added). In this case, an interference was properly declared, based on the fact that Noelle should have been granted the benefit of the February 14, 1992 filing date of the '799 application. This Court has "reasoned that once an interference has been properly declared, § 135(a) directs that the Board shall determine questions of priority." In re Gartside, 203 F.3d at 1317, 53

USPQ2d at 1776 (citing Guinn v. Kopf, 96 F.3d 1419, 1421-1422, 40 USPQ2d 1157, 1159 (Fed. Cir. 1996), cert. denied, 520 U.S. 1210 (1997)).

Although the priority issues were not fully developed before the Board, Noelle should be permitted to develop those issues in the administrative setting. A determination of priority before the Board "settles not only the rights between the parties but also rights of concern to the public. . . . To do otherwise is contrary to the PTO's mission to grant presumptively valid patents, 35 U.S.C. § 282, and thus disserves the public interest." In re Gartside, 203 F.3d at 1318, 53 USPQ2d at 1777-1778 (quoting Perkins v. Kwon, 886 F.2d 325, 328-329, 12 USPQ2d 1308, 1311 (Fed. Cir. 1989)).

To meet Congress' intent in 35 U.S.C. § 135(a) as well as to serve the public interest in the patent system, Noelle respectfully requests that interference number 104,415 be remanded to the Board for full development of the priority issues raised as a result of Noelle's February 14, 1992 constructive reduction to practice.

E. The Board Erred in Determining That There Was No Interference-in-Fact

In its final decision, the Board held that, as between Noelle's claims to the mouse CD40CR antibody and Lederman's claims to the human CD40CR antibody, no interference-in-fact existed. In doing so, the Board committed reversible error. In particular, the Board (i) applied an improper two-way obviousness test in determining whether the parties' respective inventions were patentably distinct; and (ii) without citation of authority, refused to consider relevant evidence on the issue of expectation of success contained in Noelle's specification. When the proper one-way test is utilized, and the entirety of the evidence is properly considered, the record compels the conclusion that one of ordinary skill would have had a reasonable expectation of success in making a human CD40CR MAb in view of Noelle's involved claims read in light of the teachings of the Noelle specification and the level of skill in the pertinent art. Therefore, an interference-in-fact between Noelle's mouse antibody claims and Lederman's human antibody claims exists, and the Board's holding to the contrary should be reversed.

1. The Legal Requirements For Interference-In-Fact

The Patent and Trademark Office rules relating to interferences require that, for an interference to proceed, there must be an "interference-in-fact" between claims of the parties. In particular:

> An interference-in-fact exists when at least one claim of a party that is designated to correspond to a count and at least one claim of an opponent that is designated to correspond to the count define the same patentable invention.

37 C.F.R. § 1.601(j). The rules also define "same patentable invention" as follows:

> Invention "A" is the same patentable invention as an invention "B" when invention "A" is the same as (35 U.S.C. § 102) or is obvious (35 U.S.C. § 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

37 C.F.R. § 1.601(n). Thus, to prevail on its motion, the burden was on Lederman to show that its MAb to human CD40CR invention ("invention A") was both novel and non-obvious over Noelle's invention of a MAb to mouse CD40CR ("invention B"), assuming Noelle's invention to be prior art.

2. The Board Erred in Applying a Two-Way Obviousness Test

The test applied by the Board (which the Board mischaracterized as a one-way distinctiveness test) inappropriately adds the following additional requirement to Rule 1.601(n): "and invention 'B' is the same as (35 U.S.C. § 102) or is obvious

(35 U.S.C. § 103) in view of invention 'A' assuming invention 'A" is prior art with respect to invention 'B'." The plain language of 37 CFR § 1.601 sets forth a one-way distinctiveness test, which is not the test applied by the Board. When the plain language of a regulation is not unclear, the plain language controls. Wronke v. Marsh, 787 F.2d 1569, 1574 (Fed. Cir. 1986), cert. denied, 479 U.S. 853, 107 S.Ct. 188 (1986). Based on both 37 C.F.R. § 1.601(j) and 37 C.F.R. § 1.601(n), the interference-in-fact determination should have been based on a one-way distinctiveness test.

Indeed, both this Court and the Patent and Trademark Office have applied a one-way distinctiveness test in determining interference-in-fact. For example, in Case v. CPC Int'l, Inc., 730 F.2d 745, 221 USPQ 196 (Fed. Cir. 1984), cert. denied, 469 U.S. 872 (1984), the Court stated:

> No interference in fact means that there is no interfering subject matter, that Case's patent is no impediment to granting CPC the claims of its application.

730 F.2d at 750. That is a clear statement of a one-way distinctiveness test. Further, in Hsing v. Myers, 2 USPQ2d 1861 (Bd. Pat. App. & Int. 1986) the Board considered an interference between two catalyst inventions with different ranges of sodium content. Id. at 1863. Hsing argued that there was no interference-in-fact based on the different sodium content which improved activity of the overall

catalyst. Id. He argued that this difference in sodium content, based on the unexpected results over Myers' invention, resulted in a separate patentable invention and, as a result, no interference-in-fact existed between the parties. Id. In deciding the issue, the Board stated the test pronounced in 37 C.F.R. § 1.601(n) as "[the party urging no interference-in-fact] must show that his claims define a new and non-obvious invention over that defined by [the opposing party's] claims, assuming [the opposing party's] claims are prior art with respect to [the non-moving party's] claims." Id. Thus, following the dictates of the regulations, the Board applied the necessary one-way distinctiveness test to determine if an interference-in-fact existed. Id.

The Board employed a similar analysis in Fiddes v. Baird, 30 USPQ2d 1481 (Bd. Pat. App. & Int. 1993). There, the test was restated in simpler terms as "[a] party urging that an interference-in-fact does not exist has the burden to show that its claims corresponding to the count are directed to a separate patentable invention from each of its opponents' claims designated in the notice as corresponding to the count." Id. at 1484 (citing Case v. CPC Int'l, Inc., *supra*).[8]

[8]*But see* Winter v. Fujita, 53 USPQ2d 1234, (Bd. Pat. App. & Int. 1999) in which the Board stated, without citation of authority, that "[r]esolution of an interference-in-fact issue involves a two-way patentability analysis." Id. at 1243. Because that holding of Winter is contrary to the plain language of the rules and this Court's precedential holding in Case, it is entitled to no weight on that issue.

There are significant policy reasons favoring application of a one-way test. For example, consider an interference between genus invention A and species invention B. Because a species will anticipate and render obvious a genus, In re Ruscetta, 255 F.2d 687, 689-690, 118 USPQ 101, 104 (CCPA 1958), but a genus will not necessarily anticipate or render obvious a species, In re Brouwer, 73 F.3d 380, 37 USPQ2d 1663 (Fed. Cir. 1995) under the Board's test there could generally not be an interference between genus and species inventions -- the Board's two-way test would not be met. That would lead to the absurd result of issuing separate patents to different parties for a later-invented genus and an earlier-invented species, despite the clear unpatentability of the former.[9]

In the present case, the Board misapprehended the proper test, first stating that a one-way distinctiveness test was appropriate, but then formulating and applying a two-way test:

> The question of whether there is no interference in fact is a one-way distinctiveness test. Specifically, a movant can establish that no

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[9]The Patent and Trademark Office recognized this potential problem in 1984 when the current interference rules were proposed. One comment from the public raised that very point with respect to the application of "separate patentable invention" to counts in an interference. The PTO response was that "the standard of patentability will *not* be applied 'on a mutual basis.'" (Notice of November 8, 1984; 49 FR 48432-48435; 1050 OG 401-404; original emphasis). The two-way test established in Winter and applied in this case departs from that long-established policy.

> interference in fact exists by showing that its claimed invention is patentably distinct from the opponents claimed invention. [. . .] Thus, [. . .] Lederman [the movant here] need only demonstrate that: (I) Lederman's claims are not anticipated or rendered obvious by Noelle's remaining "mouse claims; **or** (ii) Noelle's remaining "mouse" claims are not anticipated or rendered obvious by Lederman's claims."
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JA 00012.

> [O]ne skilled in the art lacked a reasonable expectation of success of obtaining Lederman's claimed "human" subject matter when provided with Noelle's "mouse" subject matter and using the screening techniques cited by Noelle. Likewise, we conclude that one skilled in the art would have lacked a reasonable expectation of success of obtaining Noelle's claimed "mouse" subject matter when provided with Lederman's claimed "human" subject matter and using these same screening methods.

JA 00027.

Thus, both by its own prior decisions and its own statement of the applicable law in this very interference, the Board applied the incorrect test for determination of interference-in-fact. As a result, the Board's decision with respect to the existence of an interference-in-fact should be vacated.

3. The Board Improperly Ignored Evidence in Noelle's Specification

In the proceedings below, neither party argued lack of novelty of one invention over the other. Thus, the interference-in-fact analysis boiled down to the question of whether Lederman's invention would have been obvious in view

of Noelle's invention and the prior art. In determining obviousness, the Board applied a two-prong test, namely, (i) whether the prior art would have motivated one of ordinary skill to make the claimed subject matter, and (ii) whether one of ordinary skill would have had an expectation of success in view of the prior art. The parties did not dispute that possession of a MAb to CD40CR of mouse provided ample motivation to obtain a MAb to CD40CR of human and vice versa (JA 0011); therefore, the sole issue on the motion was whether one of ordinary skill would have had an expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); In re Dow Chem. Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

In deciding the motion against Noelle, the Board held that there was no expectation of success of identifying activated T-cells that produced the required CD40CR antigen. Even though successful screening methods were disclosed in the Noelle specification, the Board refused to consider that evidence, holding, without citation of authority, that information in the specification cannot be considered in an interference-in-fact analysis. That was error for several reasons.

First, the Board's action is contrary to the interference rules. As shown above, 37 CFR § 1.601(n) is directed to "inventions" rather than claims, and it was error to focus on the claims to the exclusion of supporting teachings of the

specification. The Court has repeatedly held that claims are not to be read in a vacuum, but rather in light of the specification which supports them. In re Marosi, 710 F.2d 799, 802, 218 USPQ 289, 292 (Fed. Cir. 1983); In re Okuzawa, 537 F.2d 545, 548, 190 USPQ 464, 466 (CCPA 1976). There is nothing in the Rules that compels the Board's actions. It is illogical to assume that a claimed invention is in the prior art, while at the same time ignoring the very methods used by the inventor to make the invention.

Moreover, there are compelling policy reasons for rejecting the Board's interpretation of 37 CFR § 1.601(n). For example, consider the situation in which Inventions A and B are slightly different chemical compounds, with B being novel over A, but structurally obvious in view of A. Further assume that the prior art does not contain a method for making either compound. Under the Board's rationale, by refusing to consider the description of how to make A in the specification, the inventor of B could successfully argue that there would have been no expectation of success in obtaining B from A because the prior art (other than A's specification) did not teach how to make A. As a result, there would be no interference-in-fact, and two patents could issue on non-distinct inventions. To add to the absurdity, the patent on B could be invalid under 35 U.S.C. § 102(g) based on the patent to A (if A were invented earlier). Resolving such priority

conflicts is the very purpose of an interference, which would obviously be frustrated by the "rule" articulated by the Board in this case.

The Board's action was also contrary to its own precedent interpreting the interference-in-fact rules. For example, in Winter v. Fujita, 53 USPQ2d 1234 (Bd. Pat. App. & Int. 1999), the Board plainly relied on the specifications of both parties in making an interference-in-fact determination. In Winter, Fujita's claim 8 was directed to a catalyst useful for the polymerization of olefins, comprising a certain metallocene structure. Id. at 1238-39. Winter claimed overlapping metallocene compounds per se. Id. at 1236-37. The Board found that there was an interference-in-fact, interpreting Fujita's claims as covering metallocenes which can be used along with an activator to polymerize olefins. Id. at 1245-46. In response to Winter's argument that Fujita's claims should be construed as limited to a metallocene catalyst activated with aluminoxane, the Board found that even if that construction were viable, Fujita's claims would have been obvious over the Winter metallocene. In so concluding, the Board expressly considered the use to which the Winter metallocene was put, namely, mixture with an aluminoxane and subsequent use as a catalyst. Id. at 1245-46. If it is proper to consider the specification for how an invention is used, it is likewise proper to consider the specification for how an invention is made.

4. When the Noelle Specification is Considered, it Compels a Determination of Interference-In-Fact

Applying the correct test defined by a combination of 37 C.F.R. 1.601(j) and 37 C.F.R. § 1.601(n), an interference in fact exists between the '480 Noelle application claims and the '771 Lederman patent claims which correspond to the count. That is, assuming that Noelle's invention is prior art against the Lederman invention, the Lederman invention would have been obvious to one of skill in the art.

An invention is obvious under 35 U.S.C. § 103 if the prior art would (i) motivate one of ordinary skill to make the claimed invention; and (ii) provide a reasonable expectation of success. In re Vaeck, 947 F.2d at 493, 20 USPQ2d at 1442. See also, In re O'Farrell, 853 F.2d 894, 904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). Most importantly in this case, "a reasonable expectation of success, not absolute predictability supports a conclusion of obviousness." Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc., 231 F.3d 1339, 1343, 56 USPQ2d 1641, 1644 (Fed. Cir. 2000) (quoting In re Longi, 759 F.2d 887, 896, 225 USPQ 645, 651 (Fed. Cir. 1985) (internal quotation removed).

Because "[t]he parties agree that, at the relevant date, the skilled worker having anti-human CD40CR antibodies or anti-mouse CD40CR antibodies would

have been motivated to obtain the other," this factor of the obviousness analysis is not an issue here. JA 00014.

At the time of the invention of the involved parties' claims, there was a significant amount of skill in the art of monoclonal antibody production. See infra, section II.B. This level of skill, coupled with the availability of techniques used to develop monoclonal antibodies at that time, leads to a reasonable expectation of success in producing the Lederman invention following the teachings of the Noelle invention.

As of the filing date of the Noelle application, it was known in the art that both mouse and human B cells expressed CD40. See JA 02867-JA 2868; JA 02947; JA 02998-JA 03005. Because it was also known that the mouse and human CD40 antigens exhibited a conserved structure (JA 02998), it would have been reasonably expected that human activated T-cells express a homolog of the mouse CD40CR antigen. Indeed, the parties did not dispute that scientists strongly expected human CD40CR to exist on activated human T-cells based on the discovery of mouse CD40CR. See Section II(B), supra.

The Noelle application teaches one of skill in the art to use the human CD40-Ig fusion protein as a screen to locate, within the hybridoma library, those monoclonal antibodies that specifically bind mouse CD40CR and T-cells that

express mouse CD40CR. Both parties' expert witnesses testified that the human CD40-Ig fusion protein would have been expected to have bound human CD40CR with the same or greater affinity that it binds mouse CD40CR. See Section II.B, supra. Thus, because one of skill in the art would have known that mouse and human CD40CR antigens exhibited conserved structure and the logical expectation that it would bind to its natural ligand, one of skill in the art would have expected that using this same human CD40-Ig fusion protein as a screen could locate, within the hybridoma library, those monoclonal antibodies which specifically bound human CD40CR and T-cells that expressed human CD40CR[10]. See JA 02887-JA02888.

The Board improperly refused even to consider whether using this important tool would have provided a reasonable expectation of success. Its refusal was based on its "rule" that Noelle could not rely on the teachings of its own specification to show that a person of ordinary skill in possession of Noelle's invention would have had a resonable expectation of success in obtaining Mabs to human CD40CR. Citing a declaration (submitted during prosecution of the Noelle

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[10] Human CD40-Ig would compete with MAbs raised against activated human T-cells (or plasma membranes) for binding to human CD40CR. Such competitive binding reactions are powerful tools for screening hybridoma libraries to identify the desired MAbs. JA 02884-JA02885 at ¶¶ 32-33.

application) in which Dr. Aruffo testified that success in making the human CD40-Ig fusion protein would, a priori, have been unpredictable, the Board refused to give any weight to Noelle's arguments and evidence concerning the ability of this tool to identify MAbs to human CD40CR. Of course, the Noelle specification describes the preparation of the human CD40-Ig fusion protein (JA 00330-JA 00331 at section 6.1.7); therefore, the unpredictability of its production prior to Noelle's specification is irrelevant to whether the teachings of that specification provided a reasonable expectation of success in obtaining a MAb to human CD40CR.

Based on the conservation as between mouse and human antigens and the lack of invention in utilizing a well-characterized tool with a screen known and reliably practiced in the art, there was a reasonable expectation of success in arriving at the human CD40CR from the mouse CD40CR. Because both of the antibodies at issue would have bound to the target protein, in light of the Noelle invention, the Lederman invention would have been obvious. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987).

Finally, during the relevant time period, one of skill in the art was in possession of functional and competitive binding assays which would determine

the specificity of any discovered monoclonal antibody once the screening process was completed. See Section II.B, supra.

Because the whole of the experiment required to isolate the monoclonal antibody claimed by Lederman if in possession of the Noelle invention would have been obvious to one of skill in the art during the relevant time period, there exists, in this case, an interference-in-fact as defined by 37 C.F.R. § 1.601(j) and 37 C.F.R. § 1.601(n). Thus, the holding in the final opinion issued by the Board on October 19, 2001 should be reversed.

CONCLUSION

For the reasons set forth herein, Noelle respectfully requests that the Board's holding:

i) that Noelle's genus claims were not entitled to the benefit of the February 14, 1992 grandfather application;

ii) of invalidity of Noelle's genus claims under 35 U.S.C. § 102(b); and

iii) of no interference-in-fact between Noelle's mouse claims and Lederman's human claims.

should all be reversed, and the case be remanded to the Board for a priority determination.

Dated: November 29, 2002 Respectfully submitted,

E. Anthony Figg/GEK

E. Anthony Figg
~~Glenn E. Karta~~
ROTHWELL, FIGG, ERNST & MANBECK, p.c.
1425 K Street, N.W., Suite 800
Washington, D.C. 20005
Telephone: (202) 783-6040

ADDENDUM 1

Paper 108

Filed by: Michael P. Tierney
Administrative Patent Judge
Box Interference
Washington, D.C. 20231
Tel: 703-308-9797
Fax: 703-305-0942

Filed
June 28, 2001

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

RANDOLPH NOELLE
(08/742,480),

Junior Party,

v.

SETH LEDERMAN, LEONARD CHESS,
and MICHAEL J. YELLIN
(5,474,771),

Senior Party.

Patent Interference No. 104,415

Before: TORCZON, GARDNER-LANE and TIERNEY, Administrative Patent Judges.

TIERNEY, Administrative Patent Judge.

MEMORANDUM OPINION and ORDER
(Decision on Preliminary Motions)

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This interference is before a motions panel for a decision on preliminary motions. Oral argument took place on April 12, 2001. Representing Junior Party Noelle at oral hearing was R. Danny Huntington, and Mercedes Meyer. Senior Party Lederman was represented by James F. Haley, Jr., Margaret A. Pierri, and Stanley D. Liang.

Summary of the Opinion

This interference concerns CD40 counter-receptors for the CD40 B-cell antigen and monoclonal antibodies for these CD40 counter-receptors. The CD40 counter-receptors are expressed on activated T cells and are also known as CD40CRs or CD40Ls. This interference was declared with a single count having three alternative embodiments. For purposes of simplicity, the first alternative can be referred to as the "human" CD40CR and its antibody, the second alternative as "mouse" CD40CR and its antibody and the third alternative as the "genus" of CD40CRs and their antibodies. Noelle's involved application has claims directed to all three alternative embodiments whereas Lederman's involved patent presents claims directed to only the "human" embodiment. During the course of this interference, Lederman has raised several questions concerning the patentability of Noelle's "human" and "genus" claims.

At the outset, a key question posed in this interference is whether or not the isolation of CD40CR was a predictable art as of Noelle's effective filing date of February 14, 1992. We answer this question in the negative. As of February 14, 1992, the skilled artisan could not have predicted with any reasonable degree of certainty from Noelle's disclosure whether particular CD40CRs and the antibodies specific to the CD40CRs could be generated and isolated other than Noelle's disclosed mouse CD40CR and the antibodies specific to the mouse CD40CR.

We have reviewed the various motions and contingent motions presented by the parties. Of particular note, the parties raised the question of whether certain Noelle claims were adequately described and/or enabled as of Noelle's parent filing date of February 14, 1992. We have determined that Noelle did not provide an adequate written description of its "genus" and "human" claims as of February 14, 1992. As such, Noelle's claims to "human" CD40CR and the "genus" of CD40CRs and their antibodies do not receive 35 U.S.C. §120 benefit of its "earliest" applications filing date of February 14, 1992. Lederman's prior art patentability motions, however, rely upon prior art that is available under 35 U.S.C. §102(e), whether or not Noelle is entitled to a 1992 filing date. Accordingly, Lederman's preliminary motions on prior art have been deferred until final hearing to afford Noelle the opportunity to present evidence antedating the effective date of Lederman's asserted prior art.

With respect to Lederman's preliminary motions asserting Noelle's lack of patentability under 35 U.S.C. §112, first paragraph, the filing date of the involved application is the relevant date. The involved Noelle 08/742,480 ("'480 application") was filed November 1, 1996. Lederman, however, has failed to sufficiently demonstrate that Noelle's claims lack written description and/or enablement as of the filing date of the '480 application. As such, Lederman's preliminary motions regarding Noelle's alleged lack of written description and/or enablement are denied. These motions as well as others are discussed in detail below.

I. Findings of Fact

The record supports, by a preponderance of the evidence, the following findings.

A. The Interference

1. The interference involves Noelle, U.S. Application No. 08/742,480 (Noelle '480) versus Lederman et al., U.S. Patent No. 5,474,771 (Lederman '771). ("Notice Declaring Interference," Paper No. 1). Noelle is the junior party and Lederman is the senior party.

B. The Junior Party

2. The Trustees of Dartmouth College are the real party in interest in Noelle '480. (Noelle Notification Under 37 C.F.R. §1.602(b), Paper No. 6, page 1).[1] Noelle '480 was filed on November 1, 1996. Solely for the purposes of ***priority***, Noelle '480 has been accorded the benefit of the filing dates of:[2]

a. U.S. Application No. 08/338,975, filed November 14, 1994, now abandoned; and

b. U.S. Application No. 07/835,799, filed February 14, 1992, now abandoned.

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[1] It appears that IDEC Pharmaceuticals Corporation has rights in the Noelle '480 application. (Paper No. 24, pages 2-3). As set forth in the Order, Paper No. 23, the parties are to promptly update their Rule 602 statements whenever changes in interest occur. (Paper No. 23, p. 2).

[2]According priority benefit means that Noelle's earlier applications appear to be a constructive reduction to practice of the subject matter of the ***count***. *Credle v. Bond*, 25 F.3d 1566, 1570, 30 USPQ2d 1911, 1914 (Fed. Cir. 1994). For an earlier-filed application to serve as constructive reduction to practice, "the applicant must describe the subject matter of the count in terms that establish that he was in possession of the later-claimed invention, including all of the elements and limitations presented in the count, at the time of the earlier filing." *Hyatt v. Boone*, 146 F.3d 1348 at 1354, 47 USPQ2d 1128, 1131 (Fed. Cir. 1998). Further, proof of a prior constructive reduction to practice of a ***species*** would be enough evidence to prevail on priority even as to a generic invention. *Squires v. Corbett*, 560 F.2d 424, 433, 194 USPQ 513, 519 (CCPA 1977). For a discussion of the differences between priority benefit and 35 U.S.C. §120 benefit see *Cromlish v. D.Y.*, 57 USPQ2d 1318 (BPAI (ITS) 2000).

("Notice Declaring Interference," Paper No. 1, p. 45). Noelle '480 is said to be a continuation of U.S. Application No. 08/338,975 which itself is said to be a continuation of U.S. Application No. 07/835,799. (Lederman Preliminary Motion 1, Paper No. 33, p. 3).

C. The Senior Party

3. The Trustees of Columbia University in the City of New York are the real party in interest in Lederman '771 and Biogen, Inc. has been granted a license to this patent. (Lederman, Notice of Interest, Paper No. 11, p. 1). The United States of America may have rights in the '771 patent pursuant to Grant Nos. PO1-AI-26886; RO1-AI-14969 and Immunology Training Granted awarded by the National Institute of Health. (Lederman, Notice of Interest, Paper No. 11, p. 1). Lederman '771 issued from U.S. application 07/792,728 filed on November 15, 1991. (Lederman '771, LX 1001, front page).

D. The Count

4. The interference was declared on September 3, 1999, (Paper No. 1), with Count 1 which reads as follows:

> The monoclonal antibody of claim 1 of 5,474,771 or the monoclonal antibody of claim 42 or claim 51 of 08/742,480.

(Paper No. 1, p. 46).

5. Claim 1 of Lederman '771 is part of Count 1 and reads as follows:

A monoclonal antibody which specifically binds and forms a complex with the 5c8 antigen located on the surface of activated T cells and thereby inhibits T cell activation of B cells, the 5c8 antigen being an antigen to which monoclonal antibody 5c8 (ATCC Accession No. HB 10916) specifically binds.

(Lederman '771, LX 1001). For reasons of simplicity, this portion of Count 1 is referred to as the "human" embodiment.

6. Claim 42 of Noelle '480 is part of Count 1 and reads as follows:

A monoclonal antibody or fragment thereof which specifically binds to an antigen expressed on activated T cells, wherein said antigen is specifically bound by the monoclonal antibody secreted by hybridoma MR1 which hybridoma has been deposited and accorded ATCC Accession No. HB 11048.

(Noelle Clean Copy of Pending Claims, Paper No. 7, p. 2). For reasons of simplicity, this portion of Count 1 is referred to as the "mouse" embodiment.

7. Claim 51 of Noelle '480 is part of Count 1 and reads as follows:

A monoclonal antibody or fragment thereof which specifically binds CD40CR.

(Noelle Clean Copy of Pending Claims, Paper No. 7, p. 3). This portion of Count 1 is referred to as the "genus" embodiment.

8. The claims of the parties are as follows:

(i) The claims of the parties are:

Noelle '480 : 42, 43, 45-48, 50-57, 59 and 60[3]

[3]Noelle originally cited claim 58 as a pending claim. (Noelle's Clean Copy of Pending Claims, Paper No. 7). Claim 58, however, was cancelled by Examiner's Amendment during the prosecution of the '480 application. (Noelle Clarification of Status of Claim 58, Paper No. 45,

Lederman '771: 1-14

(ii) The claims of the parties which corresponded to Count 1 are:

Noelle '480 : 42, 43, 46-48, 50-54, 56, 57, 59 and 60
Lederman '771: 1-7 and 10-13

(iii) The claims of the parties which did not correspond to Count 1 are:

Noelle '480 : 45 and 55
Lederman '771: 8, 9 and 14

(Paper No. 1, p. 46).

E. Disclosures of the Application and Patent Involved in the Interference

1. Background Terminology

9. Antibodies (Ab) are a group of serum molecules produced by B lymphocytes and are a soluble form of the B cells' antigen receptor. In general, each antibody can bind specifically to just one antigen. The part of the antibody molecule that interacts with the cells of the immune system is termed the Fc portion. The part of the antibody that binds to antigen is termed the Fab portion.

10. The term "antigen" is widely used to indicate any molecule which can be specifically recognized by the adaptive elements of the immune systems that is by B cells or T cells or both. Antigens are the initiators and driving force for all adaptive immune responses.

'480 Prosecution History, Examiner's Amendment, Paper No. 10, mailed August 12, 1998).

11. CD40CR is the antigen in Lederman's '771 patent and Noelle's '480 application. The antigen CD40CR is referred to as "T-B cell activating molecule" by Lederman '771, as "glycoprotein 39" by Noelle '480, and "CD40 ligand" (CD40L) by Armitage U.S. Patent No. 5,961,974 (Armitage '974). (Kelsoe Declaration, ¶ 9, LX 1006). In particular, Lederman '771 uses the term 5c8 antigen to describe ***human*** CD40CR. Similarly, Noelle uses the term gp39 to describe ***mouse*** CD40CR antigen. (Kelsoe Declaration, ¶ 9 and 15, LX 1006).

2. The Noelle '480 Application

a. General Disclosure

12. Noelle '480 is said to describe a counter-receptor, termed CD40CR, that is expressed on activated T cells for the CD40 B-cell antigen. (Noelle '480 application, LX 1002, p. 1, lines 4-7). The antibodies for the CD40CR may be used to inhibit helper T-cell mediated activation of B-cells. (LX 1002, p. 2, line 31 to p. 3, line 4). The inhibition of B-cell activation may be useful in the treatment of the treatment of allergies or autoimmune diseases.[4] (LX 1002, p. 3, lines 14-17).

13. Noelle '480 allegedly describes a substantially purified CD40CR receptor as well as soluble ligands of the CD40CR, including antibodies or antibody fragments. (LX 1002, p. 8,

[4]An inexact but useful analogy is to think of the B-cells as having a CD40 lock, the CD40CR on an activated helper T-cell as a key for this lock and the antibody for the CD40CR as a sheath that prevents the key from fitting in the lock. By preventing the CD40CR from opening the B-cell "lock" the antibodies prevent the T-cells from activating the B-cells. (See LX 1026).

lines 1-4 and lines 18-21). In a preferred embodiment of the invention, the soluble ligand is the MR1 monoclonal antibody. (LX 1002, p. 13, lines 6-7).

14. Noelle '480 states that monoclonal antibodies can be prepared against CD40CR using any technique that provides for the production of antibody molecules by continuous cell lines in culture. (LX 1002, p. 12, lines 1-5). Lederman's expert, Dr. Kelsoe, agrees that once in possession of an antigen, such as CD40CR, a person of ordinary skill in the art could readily make a monoclonal antibody that specifically binds that antigen. (Kelsoe Declaration, LX 1006, ¶ 24).

15. Noelle '480 contends that purified CD40CR may be prepared from cells bearing CD40CR, such as activated helper T-cells, Jurkat and HSB2 cells. (LX 1002, p. 16, lines 5-8). For example, Noelle states that immunoaffinity or affinity purification could be used to isolate a particular CD40CR antigen. Specifically, Noelle '480 states that plasma membranes may be prepared from the appropriate cells by discontinuous sucrose gradient sedimentation. Purified CD40CR may then be isolated by dissociating the crude membrane extract with mild detergent and then performing size exclusion chromatography followed by affinity chromatography and/or gel electrophoresis. (LX 1002, p. 16, lines 9-18).

16. Noelle '480 also alleges that substantially purified CD40CR may be prepared from chemical synthesis or recombinant DNA techniques. (LX 1002, p. 16, lines 31-33). Specifically, Noelle '480 contends that the gene for CD40CR could be isolated by inserting cDNA prepared

from activated helper T-cells into the λgt10 expression systems, and then screened with MR1 or CD40-Ig binding to identify the CD40CR-expressing clones. (LX 1002, p. 16, line 34 to p. 17 line 3).

17. Noelle '480 describes a method for producing the MR1 monoclonal antibody through an immunization process. Specifically, the antibodies are said to be generated by a process where:

> Hamsters were immunized intraperitoneally with 5-10^6 activated T_h1 cells (D1.6) at weekly intervals for six weeks. When the serum titer against murine T_h1 was greater than about 1:10,000, cell fusions were performed with polyethylene glycol using immune hamster splenocytes and NSI. SN [supernaturant] from wells containing growing hybridomas were screened by flow cytometry on resting and activated T_h1. One particular hybridoma, which produced a mab [monoclonal antibody] that selectively recognized activated T_h, was further tested and subcloned to derive MR1.

(LX 1002, p. 13, lines 11-21 and p. 24, lines 14-26). The hybridoma identified in the Noelle '480 application as MR1 was deposited on May 22, 1992 with the American Type Culture Collection, ATCC, International Depository Authority.

18. According to Noelle '480, the ability of a ligand, such as an antibody, to bind to CD40CR may be confirmed by demonstrating that the ligand binds to the same protein as CD40-Ig or MR1.

b. Examples in Section 6

19. As depicted in Figure 3 of Noelle '480, a CD40-Ig was said to have detected a molecule expressed on activated, but not resting, T_h. (LX 1002, p. 6, lines 14-15 and Fig. 3). In

particular, Noelle is said to have stained resting and activated T_h1 with CD40-Ig or CD7E-Ig followed by FITC-anti-HIgG. (LX 1002, p. 28, lines 8-11). The T_h1 that were activated with anti-CD3 stained 56% positive with CD40-Ig, but not on the resting T_h1 or the control CD7E-Ig. (LX 1002, p. 28, lines 13-16).

20. As depicted in Figure 4 of Noelle '480, a CD40-Ig was said to have immunoprecipitated a 39 kD protein from lysate of activated T_h1. A CD7E-Ig control did not. (LX 1002, p. 6, lines 24-30 and p. 28, lines 16-30, Figure 4).

21. MR1 and CD40-Ig are said to have recognized the same molecule expressed on activated T_h. (LX 1002, p. 7, lines 6-7, Figure 6). As depicted in the table of Noelle '480 Figure 6, MR1 appears to block the human CD40-Ig from binding to activated mouse T_h cells in a dose dependent manner. (LX 1002, Figure 6, Table and p. 28, line 35 to p. 29, line 10). In contrast, a hamster anti-T cell monoclonal antibody control did not block the binding of the human CD40-Ig. (LX 1002, p. 29, lines 8-10). According to Noelle '480, this data suggested that CD40-Ig and MR1 recognized overlapping or identical epitopes on the 39 kD T_h protein. (LX 1002, p. 29, lines 11-13).

22. To demonstrate that CD40-Ig and MR1 recognized the same molecule, Noelle allegedly identified the antigen that bound MR1 by immunoprecipitation of proteins from radiolabelled T_h lysates. (LX 1002, p. 29, lines 13-16). Both the CD40-Ig and MR1 are said to have immunoprecipitated a 39 kD protein. (LX 1002, p. 29, lines 13-16 and Figure 6b).

(LX 1002, p. 31, lines 20-31).

26. Section 7 of the Noelle '480 application does not report a control demonstrating that the observed binding is specific and due to the CD40 moiety rather than the Ig moiety on the fusion protein.

3. The Lederman '771 Patent

27. Lederman '771 relates to a monoclonal antibody that specifically recognizes and forms a complex with T-B cell activating molecule (aka, T-Bam, CD40L, CD40CR), a protein located on the surface of activated T cells and thereby inhibits T cell activation of B cells. (LX 1001, Abstract, col. 2, lines 16-23, LX 1006, ¶ 43). In particular, Lederman '771 provides the monoclonal antibody 5c8, ATCC Accession No. HB 10916. (LX 1001, Abstract).

28. Lederman '771 is said to have raised 5c8 monoclonal antibodies against a mutant human T cell leukemia cell line designated D1.1. Specifically, Lederman '771 describes characterizing cell surface proteins on activated $CD4^+$ T cells that mediate helper effector function. Mice were immunized with the D1.1 clone of Jurkat and monoclonal antibodies were generated. The hybridoma supernatants were screened for differential binding to the D1.1 clone and a non-helper Jurkat clone, B.27. From this, Lederman '771 is said to have identified a murine IgG2a mAb, termed 5c8, that bound specifically to the surface of D1.1 cells and not to the surface of the non-helper, B2.7 cells. (LX 1001, Example 3, col. 21, lines 35-48).

29. Lederman '771 is said to have studied the effect of mAb 5c8 in assays of D1.1 induced CD23 expression on B cells. According to Lederman '771, the mAb 5c8 "potently" inhibited Jurkat D1.1 induced cell activation. In contrast, the isotype control mAb, W6/32 did not inhibit the D1.1 mediated B cell activation. Lederman '771 states that the data suggests that the 5c8 Ag plays a critical role in the helper effector function of the D1.1 cells. (LX 1001, Example 3, col. 22, lines 20-29 and Figures 8A-L).

30. Lederman '771 is said to provide a pharmaceutical composition comprising the monoclonal antibody and a pharmaceutically acceptable carrier. (LX 1001, col. 7, lines 61-63). Additionally, Lederman '771 states that methods for determining an "effective amount" of the pharmaceutical composition comprising the antibody are well known to those skilled in the art and will depend upon factors including, but not limited to, the type of animal involved and the animal's body weight. (LX 1001, col. 10, line 67 to col. 11, line 17).

F. Additional Findings of Fact

1. Ordinary Skill in the Art

31. Both Lederman and Noelle's experts appear to agree that, as of February 14, 1992, the person skilled in the art was familiar with the requirements for generating immune responses, including humoral and cellular responses, the cell types and interactions between such cells involved in the establishment of said immune responses and the relevant molecules responsible for such interactions. The person skilled in the art would also have been familiar with the concepts of antigen presentation and factors augmenting or suppressing immune responses. In

addition, that person would have been familiar with methods for generating monoclonal antibodies which specifically bind protein antigens, including monoclonal antibodies which modify immune responses. (LX 1007, Shevach Declaration, ¶ 10; LX 1006, Kelsoe Declaration, ¶ 8 and NX 2012, Clark Declaration ¶ 7).

2. Isolation and Purification of CD40CR

32. As of February 14, 1992, the isolation and purification of CD40 counter receptors ("CD40CR") was ***not*** a predictable art. As of this date, the skilled artisan could not have predicted with any reasonable degree of certainty from Noelle's disclosure whether particular CD40CRs and the antibodies specific to the CD40CRs could be generated and isolated other than Noelle's disclosed mouse CD40CR and the antibodies specific to the mouse CD40CR. Indeed, it would have been difficult for the skilled artisan to generate and isolate the CD40CRs and antibodies specific to the CD40CRs beyond those disclosed by Noelle's application. (See generally, LX 1006, LX1007, LX 1092 and LX 1093).

33. As of February 14, 1992, the construction of CD40-Ig fusion protein, such as Noelle's CD40-Ig, would have been extremely difficult. (LX 1092, ¶ 16, LX1093, ¶ 10). During the prosecution history of Noelle's parent U.S. Application No. 07/835,799, Dr. Sandro Aruffo submitted a declaration stating that:

> Prior to the actual construction of the CD40-immunoglobin fusion protein disclosed and claimed in the above-identified patent application [07/835,799], I and my co-inventors could not predict whether this approach would result in a biologically active fusion protein.

(Declaration of Aruffo under 37 C.F.R. 1.132 dated July 7, 1994, LX 1009, p. 2). Dr. Aruffo further stated that:

> [E]ach individual fusion protein must be constructed independently, and whether a particular fusion protein can be successfully generated is often not determinable until the experiment is performed. In view of this lack of predictability, there is not a reasonable expectation of success prior to the actual production of a recombinant immunoglobin fusion molecule.

(Declaration of Aruffo under 37 C.F.R. 1.132 dated July 7, 1994, LX 1009, p. 3).

3. The Noelle '480 Application Requires One Skilled in the Art to Make Numerous Assumptions

34. The Noelle '480 application requires that one skilled in the art make certain assumptions as to non-mouse CD40CRs and their antibodies. For example, Noelle '480 does not describe the structure that is common to both mouse and human CD40CR that is essential for a common function of the two proteins. Yet, Noelle's expert, Dr. Clark, states that:

> Based on the foregoing, I believe that ***it is more likely than not*** that [1] non-mouse CD40CRs would be expressed on the surface of non-mouse activated T-cells, e.g., human and other non-mouse vertebrate T-cells; [2] that such receptor would possess a similar, but not identical, molecular weight as mouse CD40CR; [3] that non-mouse CD40CR would possess a similar but not identical structure as mouse CD40CR; [4] that non-mouse CD40CR would possess a similar function, i.e., would induce T-cell activation of B-cells; [sic] by binding to CD40 and [5] that an antibody to non-mouse CD40CR receptor would have a similar biological effect to MR1 in its homologous species, i.e., would inhibit T-cell dependent/B-cell activation.

(NX 2012, ¶ 19, emphasis added).

35. One skilled in the art reviewing the Noelle '480 application would have doubts regarding the validity of Section 7. Specifically, a control should have been included in Section 7 to confirm that the reported binding is due to the CD40 moiety, rather than the Ig moiety, of the CD40-Ig fusion protein. (LX1007, ¶ 39, LX 1006, ¶ 30). Absent the proper control, one skilled in the art could not have known whether the CD40-Ig fusion protein was binding to a cell surface protein on Jurkat and HSB2 cells via the CD40 portion of the CD40-Ig molecule. (LX1007, ¶ 39, LX 1006, ¶ 30). At best, Noelle's expert, Dr. Clark, states that:

> In my opinion, ***it is more plausible than not to assume that the results in Section 7 and Figure 7 are valid***, e.g., attributable to the CD40 portion of the fusion protein as the Noelle application describes several other experiments (described in Section 6.2.3 of Noelle Application), wherein an appropriate control, i.e., CD7E-Ig was utilized and confirmed that the observed binding of the CD40-Ig to activated mouse T helper cells and CD40, and not the Ig moiety of the fusion protein.

(NX 2012, ¶ 14, emphasis added).

36. As of February 14, 1992, it would have been difficult for one of ***ordinary*** skill in the art to conduct the expression cloning methodology recited in the Noelle '480 application. (Amendment and Response filed October 1, 1993 in support of Armitage, U.S. Application No. 07/969,703, LX 1083, p. 7, LX 1092, ¶ 45 on p. 17, LX 1093, ¶ 33).

II. Opinion

A. Overview of Preliminary Motions

There are eleven outstanding preliminary motions awaiting decision. Specifically, there are seven preliminary motions filed by Lederman (Lederman Preliminary Motions 1-7) and four

by Noelle (Noelle Preliminary Motions 1-4). Of the seven Lederman Preliminary Motions, Preliminary Motions 1 through 5 move for judgement under 37 CFR §1.633(a) on the grounds that certain claims of Noelle are unpatentable. Specifically, Lederman Preliminary Motions 1 and 2 allege unpatentability due to prior art, Preliminary Motion 3 alleges a lack of written description, Preliminary Motion 4 alleges a lack of enablement, and Motion 5 alleges a failure to particularly point out and distinctly claim the subject matter that Noelle regards as his invention.[5] Additionally, Lederman Preliminary Motions 6 and 7 request that the interfering subject matter be redefined and are contingent upon the grant, in whole or in part, of any one of Lederman's Preliminary Motions 1-5.[6] Similar to Lederman Preliminary Motions 6 and 7, Noelle Preliminary Motions 1 and 3 are contingent motions requesting that the interfering subject matter be redefined. Additionally, Noelle Preliminary Motions 2 and 4 are contingent upon the granting of Noelle Preliminary Motions 1 and 3, respectively, and request priority benefit of U.S. Application 07/835,799, filed February 14, 1992.

Additionally, Lederman has objected to the admissibility of certain evidence submitted by Noelle. (Lederman Objections to Admissibility of Noelle Evidence, Paper No. 74). Lederman's objections are primarily directed to specific paragraphs contained in Noelle's

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[5]A chart correlating Lederman's Preliminary Motions 1-5 and the Noelle claims alleged to be unpatentable is attached as Appendix I.

[6]During oral hearing counsel for Lederman indicated that Lederman Preliminary Motions 6 and 7 were no longer contingent upon the grant, in whole or part, of any one of Lederman Preliminary Motions 1 through 5. (April 12, 2001, Hearing Transcript, p. 8, line 12 to p. 9, line 22). Lederman's counsel did not provide any citation to where in the record the contingent status of Preliminary Motions 6 and 7 was changed. Moreover, a review of the record failed to reveal any change in the contingent status of Lederman Preliminary Motions 6 and 7.

Oppositions 3 and 5. Moreover, Lederman's objections are that the cited paragraphs are irrelevant or unsupported. Indeed, the only specific citation and objection to a Noelle exhibit is that it is "irrelevant." (Paper No. 74, p. 2). Lederman's objections are noted.

1. Lederman's Preliminary Motions

a. Lederman Preliminary Motion 1

Lederman Preliminary Motion 1 requests judgment against Noelle claims 42, 43, 46, 47, 51-53, 57, 59 and 60 on the grounds that they are unpatentable. Specifically, Lederman argues that Noelle's claims are either anticipated under 35 U.S.C. §102(e) or rendered obvious under 35 U.S.C. §103 by Armitage, U.S. Patent 5,961,974 (LX 1003).[7] (Lederman Preliminary Motion 1, Paper No. 33, p. 2).

As noted by Lederman, Armitage U. S. Patent 5,961,974 ('974 patent) issued on October 5, 1999 from (1) application 08/249,189, filed May 24, 1994, which is said to be a continuation-in-part of (2) application 07/969,703, filed October 23, 1992, which itself is said to be a continuation-in-part of (3) application 07/805,723 ('723 application), filed *December 5, 1991*, which is said to be a continuation-in-part of (4) application 07/783,707 ('707 application), filed *October 25, 1991*. The two latter dates precede the February 14, 1992 priority date accorded to Noelle in this interference. Based on these two earlier filing dates, Lederman alleges that the Armitage '974 patent is available as prior art to Noelle under 35 U.S.C. §102(e). (Paper No. 33, ¶ 14).

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[7]See Appendix 1 of Paper No. 33 for a comparison of the '974 patent and claims 42, 43, 46, 47, 51, 52, 53, 57, 59 and 60 of Noelle '480.

During prosecution of the Armitage '974 patent, the Examiner accorded Armitage benefit of the October 25, 1991 filing date for monoclonal antibodies specific for mouse CD40 ligand (mouse CD40CR) and accorded Armitage benefit of the December 5, 1991 filing date for monoclonal antibodies specific for human CD40 ligand (human CD40CR). (LX 1040, '189 Application Prosecution History, Paper No. 7, September 18, 1995 Office Action, p. 3).

According to Lederman, prior to Noelle's priority date of February 14, 1992, Armitage described the isolation and sequencing of mouse CD40 ligand (mouse CD40CR) and human CD40 ligand (human CD40CR) and identified them as polypeptides that bind to the extracellular binding region of CD40 on antigen presenting cells, such as B cells. (Paper No. 33, fact no. 15). Furthermore, Lederman alleges that, prior to Noelle's priority date, Armitage described and enabled (1) mouse CD40 ligand (mouse CD40CR) and a monoclonal antibody that specifically binds mouse CD40 ligand (mouse CD40CR) and (2) human CD40 ligand (human CD40CR) and a monoclonal antibody that specifically binds human CD40 ligand (human CD40CR). (Paper No. 33, fact no. 18). Noelle admits, i.e., does not deny, Lederman's statement of material facts 1-12 and 14-19. (Noelle Opposition 1, Paper No. 57, pages 1-2).

Rather than distinguish Noelle's claims from the teachings of the '974 patent, Noelle merely states that Noelle has a date of invention prior to the effective date of the '974, and thus, the '974 patent would not be prior art to Noelle. (Paper No. 57, page 4). As such, Noelle has requested that Lederman Preliminary Motion 1 be deferred until final hearing and decided after the presentation of Noelle's priority case. (Paper No. 57, page 4).

In a telephone conference on May 22, 2000, Administrative Judge Torczon agreed to defer Lederman's Preliminary Motion 1 until Noelle's priority case had been presented. At the

April 12, 2001 hearing, Noelle's counsel confirmed that, with respect to Lederman Preliminary Motions 1 and 2, "all that got deferred was the antedating effort." (April 12, 2001, Hearing Transcript, p. 78, line 21 to p. 79, line 22). Accordingly, Lederman Preliminary Motion 1 is ***deferred*** solely to afford Noelle the opportunity to present evidence antedating the effective date of the '974 patent.

b. Lederman Preliminary Motion 2

Lederman Preliminary Motion 2 requests judgment against Noelle claims 51, 52, 56, 59 and 60 on the grounds that they are unpatentable. Specifically, Lederman argues that Noelle's claims are anticipated under 35 U.S.C. §102(e) by Lederman '771 (LX 1002). (Lederman Preliminary Motion 2, Paper No. 34, p. 2).

The '771 patent issued on December 12, 1995 from application 07/792,728, filed November 15, 1991. (Paper No. 34, fact 11). According to Lederman, Noelle's claims have an effective filing date of February 14, 1992. (Paper No. 34, fact 8). Lederman contends that the '771 patent is prior art to Noelle as the Lederman '771 filing date precedes Noelle's effective filing date. (Paper No. 34, fact 11).

According to Lederman, '771 patent disclosed and enabled monoclonal antibodies, such as monoclonal antibody 5c8, which specifically bind 5c8 antigen (human CD40CR antigen). (Paper No. 34, fact 13). Lederman also alleges that the '771 patent disclosed and enabled the hybridoma cell line that produces monoclonal antibody 5c8 . (Paper No. 34, fact 13). This cell line was deposited on November 14, 1991 under accession number HB 10916. (Paper No. 34, fact 13).

Lederman states that the '771 patent disclosed and enabled the D1.1 cell line, a human CD4 T cell leukemia cell line to which the monoclonal antibody 5c8 specifically binds. (Paper No. 34, fact 14). Lederman further states that the '771 patent identified the 5c8 antigen, a 30 kilodalton D1.1 surface protein to which monoclonal antibody 5c8 specifically binds. (Paper No. 34, fact 14). The '771 patent is said to disclose the expression of the 5c8 antigen on activated human T cells. (Paper No. 34, fact 15).

According to Lederman, the D1.1 cell line was deposited with the American Type Culture Collection on November 14, 1991, under accession number CRL 10915. (Paper No. 34, fact 14). Additionally, Lederman alleges that the '771 patent functionally characterized the D1.1 surface protein by demonstrating that the 5c8 antigen is required for T cell-dependent B cell activation. (Paper No. 34, fact 16).

Additionally, Lederman states that the '771 patent disclosed and enabled pharmaceutical compositions comprising monoclonal antibody 5c8 and a pharmaceutically acceptable carrier. (Paper No. 34, fact 17). Lederman contends that the '771 patent teaches that methods for determining an "effective amount" of the antibody depends on factors including, but not limited to, the type and body weight of the animal to be treated. (Paper No. 34, fact 17).

Lederman also alleges that the '771 patent disclosed and enabled a method for detecting the presence of a T cell tumor. (Paper No. 34, fact 18). According to Lederman the method involves administering to a patient an effective imaging amount of a pharmaceutical composition comprising monoclonal antibody 5c8, bound to a detectable marker that is effective for binding to a protein (i.e., 5c8 antigen) on the surface of T cell tumor cells under conditions that permit the formation of complexes between the monoclonal antibody and the protein. (Paper No. 34,

fact 18). The '771 patent is said to define an "effective amount" of the pharmaceutical composition as an amount effective to detect the presence of a T cell tumor in the patient. (Paper No. 34, fact 18). The amount is said to depend upon such factors as: the type of patient involved, the size of the blood sample contacted and the detectable marker used. (Paper No. 34, fact 18).

Based upon the above "facts," Lederman concludes that Noelle claims 51, 52, 56, 59 and 60 are anticipated by the '771 patent. (See, Paper No. 34, pages 12-16).

Noelle admits, i.e., does not deny, Lederman's statement of material facts 1-9, 11-12 and 14-21. (Noelle Opposition 2, Paper No. 58, pages 2-3). Indeed, rather than distinguish Noelle's claims from the teachings of the '771 patent, Noelle merely states that Noelle has a date of invention prior to the effective date of the '771, and thus, the '771 patent would not be prior art to Noelle. (Paper No. 58, page 4). As such, Noelle has requested that Lederman Preliminary Motion 2 be deferred until final hearing and decided after the presentation of Noelle's priority case. (Paper No. 58, page 4).

In a telephone conference on May 22, 2000, Administrative Judge Torczon agreed to defer Lederman's Preliminary Motion 2 until Noelle's priority case had been presented. At the April 12, 2001 hearing, Noelle's counsel confirmed that, with respect to Lederman Preliminary Motions 1 and 2, "all that got deferred was the antedating effort." (April 12, 2001, Hearing Transcript, p. 78, line 21 to p. 79, line 22). Accordingly, Lederman Preliminary Motion 2 is ***deferred*** solely to afford Noelle the opportunity to present evidence antedating the effective date of the '771 patent.

c. Lederman Preliminary Motion 3

Lederman Preliminary Motion 3 requests judgement against Noelle claims 51, 52, 53, 56, 59 and 60 on the grounds that they are unpatentable to Noelle under the written description requirement of 35 U.S.C. §112, first paragraph. (Lederman Preliminary Motion 3, Paper No. 35, p. 2). Specifically, Lederman contends that the Noelle '480 application does not disclose an isolated and fully characterized CD40CR antigen from any non-mouse source or any identifying characteristic of such an antigen.

i. Case Law Analysis for Written Description Requirement

While the specifics of the cases concerning adequate written description vary, the cases agree that the inquiry is *factual* and must be assessed on a *case-by-case* basis. Moreover, because of the fact-sensitive nature of the written description inquiry, the Federal Circuit has advised against misapplication of precedent in this area. *See, Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 1000, 54 USPQ2d 1227, 1235 (Fed. Cir. 2000); *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); and, *In re Driscoll*, 562 F.2d 1245, 1250, 195 USPQ 434, 438 (CCPA 1977).

The purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by the inventor. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116. The inventor can demonstrate possession by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention. The inventor, however, needs to show that the inventor was "in possession" of the invention by describing the invention, with

all its claimed limitations, not that which makes it obvious. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1571, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

The disclosure as originally filed does not have to provide *ipsis verbis* support for the claimed subject matter at issue. *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000); *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570, 39 USPQ2d 1895, 1904 (Fed. Cir. 1996). Rather, if the written description does not use precisely the same terms used in a claim, the question then is whether the specification directs or guides one skilled in the art to the subject matter claimed such that the specification reasonably conveys to those skilled in the art that the inventor invented what is claimed. *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570, 39 USPQ2d 1895, 1904 (Fed. Cir. 1996); *Vas-Cath Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116; *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

In making our factual inquiry into Noelle's written description, the decision in *Regents of University of California v. Eli Lilly & Co.*[8] ("*Lilly*") is particularly instructive. In *Lilly* the Federal Circuit addressed the question of adequate written description of DNA. Specifically, *Lilly* involved an infringement suit which, among other things, concerned the validity and enforceability of Rutter *et al.*, U.S. Patent 4,625,525 ("'525 patent"). Claim 1 of the '525 patent was directed toward a vertebrate insulin-encoding cDNA plasmid. Claim 5 of the '525 patent depended from claim 1 and was limited to human insulin cDNA. *Id.* at1563, 43 USPQ2d at 1401. The district court had ruled that all the asserted claims of the '525 patent, i.e., claims 1, 2 and 4-7, were invalid under 35 U.S.C. 112, first paragraph as "the specification, although it

[8]119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

provided an adequate written description of rat cDNA, did not provide an adequate written description of the cDNA required by the asserted claims." *Id.* at1566, 43 USPQ2d at 1404.

The Federal Circuit affirmed the district courts ruling that claims 1, 2 and 4-7 of the '525 patent were invalid for lack of written description. At the outset, the Court stated that:

> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606.

Id.

Having discussed the general principles surrounding questions of adequate written description, the Court then considered the validity of claim 5, which was specific to human insulin cDNA. The Court noted that the '525 patent described a method of obtaining this cDNA by means of a constructive example, Example 6. The Court concluded that:

> This example, however, provides only a general method for obtaining the human cDNA (it incorporates by reference the method used to obtain the rat cDNA) along with the amino acid sequences of human insulin A and B chains. Whether or not it provides an enabling disclosure, it does not provide a written description of the cDNA encoding human insulin, which is necessary to provide a written description of the subject matter of claim 5. The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Id. at 1567, 43 USPQ2d at 1405.

Dispensing with species claim 5, the Court then focused on the vertebrate and mammalian genus claims. With respect to the genus, the Court stated:

> A written description of an invention involving a chemical genus, like a description of a chemical species, "requires a precise definition, such as by structure, formula, [or] chemical name," of the claimed subject matter sufficient to distinguish it from other materials. *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . .").

Id. at 1568, 43 USPQ2d at 1405. Moreover, the Court determined that definition by function alone did not suffice to describe a claimed genus. Specifically, the Court held that:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*[9]). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed.

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[9] *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991).

> Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Id. at 1568, 43 USPQ2d at 1406. Accordingly, the Court concluded that the general language of the '525 patent's written description supported only the specific nucleotide of rat insulin and did not support the claimed genera of vertebrate and mammalian cDNA. *Id.* at 1569, 43 USPQ2d at 1406.

ii. Noelle Claims 51, 52, 53, 56, 59 and 60 Lack Written Descriptive Support as of February 14, 1992

For all practical purposes, Noelle claims 51, 52, 53, 56, 59 and 60 can be divided into three groups: (1) human CD40CR and its antibodies; (2) murine CD40CR's and their antibodies; and (3) the genus of CD40CR's and their antibodies. Generally, Lederman argues that as of February 14, 1992, Noelle does not describe an isolated and fully characterized CD40CR antigen from any non-mouse source or any identifying characteristic of such CD40CR antigen. (Lederman Preliminary Motion 3, Paper No. 35, fact 22). Moreover, as to the CD40CR genus and the murine subgenus, Lederman argues that Noelle does not provide information on structure common to the genus or subgenus and does not provide a reliable source or a pro-form of human CD40CR or any other CD40CR other than mouse. (Paper No. 35, p. 22). As for the human CD40CR, Lederman contends that the Noelle disclosure relating to CD40CR on human cells is lacking in controls and fails to reasonably convey to those of ordinary skill in the art that Noelle "possessed" the human CD40CR and its specific antibodies. (Paper No. 35, pages 15-19). We find that Lederman has presented credible and convincing evidence that the Noelle's claims fail

to satisfy the written description requirement of 35 U.S.C. §112, first paragraph as of February 14, 1992.

Noelle argues that a written description analysis in the present case requires different considerations than those addressed in *Lilly*. (Noelle Opposition 3, Paper No. 59, p. 20). For instance, Noelle contends that there exists over a decade of technological developments between the relevant date of *Lilly* and Noelle's February 14, 1992 priority date. (Paper No. 59, pages 15-16 and 20). Also, Noelle argues that Lilly is directed toward cDNAs whereas Noelle is directed to antibodies. (Paper No. 59, p. 20). We find these distinctions unpersuasive. Like *Lilly*, Noelle's claimed invention, as of February 14, 1992, involved an unpredictable technology. As with *Lilly*, Noelle presents claims to a genus and to a particular species, human, while describing only one species (mouse). Indeed, the specifications in both *Lilly* and Noelle fail to describe any structural features commonly possessed by the member of the genus that distinguish them from others such that one skilled in the art may recognize the identity of the members of the genus. Further, with respect to the human CD40CR claims, Noelle provides an alleged process for obtaining the human CD40CR but fails to sufficiently define the structural or physical characteristics of the human CD40CR. As with *Lilly*, we conclude that the written description requirement necessitates a description of the invention, not an indication of a result that one might achieve if one made that invention. *Lilly* at 1568, 43 USPQ2d at 1406.[10]

Noelle contends that the written description requirement is satisfied by the description of functional characteristics coupled with a known correlation between structure and function and

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[10]If the written description principles set forth in *Lilly* cannot be extended to other unpredictable biotechnical arts, our decision regarding Noelle's lack of written description would need to be reassessed.

that this correlation did not exist for the University of California in the *Lilly* decision. (Paper No. 59, p. 15). Noelle, however, does not appear to have identified a specific correlation between the structure of CD40CR antibodies and their function. Moreover, at oral hearing, Noelle's counsel agreed that Noelle's specification identifies the CD40CR antibodies by functional similarity rather than structural similarity.[11, 12] Furthermore, as pointed out by Lederman, Noelle's application does not sufficiently define the common structural or physical characteristics between the disclosed mouse CD40CR and any other CD40CR. (Lederman Reply 3, Paper No. 80, p. 10; LX 1093, ¶ 46).

Additionally, Noelle disputes that the only disclosure in the Noelle application relating to human CD40CR was flawed. For instance, Noelle states that although the '480 application did not report verifying the conformation of the CD40 moiety using CD40 antibodies, control experiments were conducted that confirmed that the binding of human CD40-Ig was specific and

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[11] Judge Tierney: What is the structural similarity between each of the monoclonal antibodies fitting within the genus of the third alternative [of the count]?
Mr. Huntington (Noelle): There is some structural similarity.
Judge Tierney: And what is that?
Mr. Hunntington: I can't describe it to you, and I don't think it's important in this sense. It's important that there is a recognized definition of CD40CR.

(Hearing Transcript, page 37, line 18 to p. 38, line 7).

[12] Judge Tierney: We're really not saying there is a structural similarity except in fact that there is a functional similarity.
Mr. Huntington: That's right. Well, there is somewhat a structure and function similarity, but, indeed you're identifying it by function. That's how you go through and identify the materials.

(Hearing Transcript, page 38, line 14 to line 22).

not attributable to the Ig portion of the molecule. (Paper No. 59, pages 19-20, citing the ¶¶ 6-10 of the Declaration of Laura Grosmaire, LX 2010). At the outset, Noelle fails to explain the relevance of control experiments that ***were not described*** in the Noelle specification. Further, Noelle has failed to convince us that such experiments were actually conducted. Laura Grosmaire's declaration testimony specifically states "[w]hile I cannot say with any degree of certainty that I conducted the particular experiment contained in Figures 7A-7C, it is quite possible that I did." (NX 2010, Grosmaire Declaration, ¶ 6). Laura Grosmaire further testified that "I have noted that the flow cytometry experimental result contained in Figures 7A-7C does not contain a negative control wherein the binding of the cell to an irrelevant Ig fusion protein was tested." (NX 2010,¶ 7). Laura Grosmaire then provided three different explanations for the absence of such a control. One explanation was that "a negative control was not effected." (NX 2010,¶ 7).

iii. Noelle Claims 51, 52, 53, 56, 59 and 60 Lack Benefit Under 35 U.S.C. §120 of Noelle's Parent 07/835,799 Application

Our decision that Noelle claims 51, 52, 53, 56, 59 and 60 lack written description as of February 14, 1992 compels a conclusion that these claims do not receive benefit under 35 U.S.C. §120 of Noelle's parent '799 application. *Applied Materials Inc. v. Advanced Semiconductor Materials*, 98 F.3d 1563, 40 USPQ2d 1481, 1494 (Fed. Cir. 1996) (To secure the benefit of the filing date of an earlier filed ("parent") application, 35 U.S.C. §120 requires that the claimed invention be disclosed in the manner provided by the first paragraph of §112, which requires 1) a written description of the invention, 2) enablement, and 3) disclosure of the best mode for

practicing the invention.). Lacking benefit under 35 U.S.C. §120, Noelle's effective date of filing for claims 51, 52, 53, 56, 59 and 60 is, at best, the filing date of the parent '975 application, November 14, 1994, or the filing date of the '480 application November 11, 1996.

Lacking benefit of the February 14, 1992 filing date of its parent '799 application does not alter our decision to defer Lederman Preliminary Motion 1, unpatentability under 35 U.S.C. §102(e) and under §103 over Armitage '974. Specifically, the Armitage '974 patent issued on October 5, **1999** and both Lederman and Noelle agreed that the Armitage '974 patent is *prima facie* available as prior art to Noelle under 35 U.S.C. §102(e) by reason of its parent filing dates of December 5, 1991 and October 25, 1991. (Paper No. 33, fact 14, Paper No. 57, page 2, Noelle admission of fact 14). Thus, Armitage '974 is available as prior art to Noelle '480 under 35 U.S.C. §102(e) and is not a statutory bar under 35 U.S.C. §102(b), whether or not Noelle is accorded benefit of its February 14, 1992 filing date.

Similarly, lacking benefit of the February 14, 1992 filing date does not alter our decision to defer Lederman Preliminary Motion 2, unpatentability under 35 U.S.C. §102(e) over Lederman '771. In particular, Lederman '771 issued on December 12, **1995**. Both Lederman and Noelle agreed that the Armitage '974 patent is *prima facie* available as prior art to Noelle under 35 U.S.C. §102(e) by reason of its filing date of November 15, 1991. Whether or not Noelle is accorded benefit of its February 14, 1992 date, Lederman '771 remains available as prior art to Noelle '480 under 35 U.S.C. §102(e) and is not a statutory bar under 35 U.S.C. §102(b).

iv. Written Descriptive Support for Patentability is Determined as of Filing Date of Application

According to both Lederman and Noelle, the relevant date for determining the compliance of the Noelle '480 application with the written description requirement is February 14, 1992, the filing date of Noelle's parent 07/835,799 application ("'799 application"). (Paper No. 35, fact 7, Noelle Opposition 3, p. 1, admits Lederman fact 7). Yet, compliance with 35 U.S.C. §112, first paragraph is as of the filing date of the application relied on. *Microsoft v. Reiffin*, 214 F.3d 1342, 54 USPQ2d 1915 (Fed. Cir. 2000) (If claims to subject matter in later-filed application are not supported by ancestor application in terms of 35 U.S.C. §112, first paragraph, they are simply denied benefit of earlier filing date, not invalidated. Thus, for purposes §112, first paragraph, earlier specifications are relevant only when the benefit of an earlier filing date is sought under 35 U.S.C. §120.); *Vas-Cath Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116. The filing date of the relied on Noelle '480 application is November 1, 1996. Accordingly, the date for compliance with the written description requirement for the Noelle '480 application is November 1, 1996.

Lederman is the moving party for Lederman Preliminary Motion 3, and as such bears the burden of proof with respect to this motion. 37 CFR §1.633(a). Lederman, however, has failed to demonstrate that Noelle's claims lack written descriptive support as of November 1, 1996.[1] As such, Lederman Preliminary Motion 3 is ***denied***.

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[1] One of Lederman's arguments in applying the principles set forth in *Lilly* is the unpredictability of isolating and purifying CD40CRs as of February 14, 1992. It is not clear on the record before us whether the isolation and purification of CD40CRs was an unpredictable art as of November 1, 1996.

It is well settled that the enablement requirement is separate and distinct from the written description requirement of §112, first paragraph, and that a specification may enable one skilled in the art to make and use an invention and yet still not describe it. *Vas-Cath*, 935 F.2d at 1562-1563, 19 USPQ2d at 1115, 1117. Accordingly, our denial of Lederman Preliminary Motion 3 is not dispositive as to the question of Noelle's enablement or lack thereof for its "human" and "genus" claims.

d. Lederman Preliminary Motion 4

Lederman Preliminary Motion 4 requests judgement against Noelle claims 42-43, 47-48, 50-54, 56 and 59-60 on the grounds that they are unpatentable to Noelle under the enablement requirement of 35 U.S.C. §112, first paragraph. (Lederman Preliminary Motion 4, Paper No. 36, p. 2). Specifically, Lederman contends that as to claims 42-43, 47-48 and 50-54, the Noelle '480 application does not provide an enabling disclosure for antibody fragments that specifically bind CD40CR antigens. (Paper No. 36, fact 15 and p. 11). Also, as to Noelle claims 51-53, 56 and 59-60, Lederman contends that Noelle '480, as of February 14, 1992, does not enable monoclonal antibodies that bind any non-mouse CD40CR antigens. (Paper No. 36, p. 10).

According to both Lederman and Noelle, the relevant date for determining the compliance of the Noelle '480 application with the enablement requirement is February 14, 1992, the filing date of Noelle's parent '799 application. (Paper No. 36, facts 2 and 3, Noelle Opposition 4, p. 1, admits Lederman facts 2 and 3). As discussed above, the filing date under 35 U.S.C. §112, first paragraph is the filing date of the involved '480 application, i.e., November 1,

1996. As Lederman has failed to file any preliminary motions citing prior art having an effective date falling between the filing date of the Noelle '480 application and the parent '799 application, we do not reach the issue of enablement for Noelle's parent '799 filing date of February 14, 1992.

Lederman is the moving party for Lederman Preliminary Motion 4, and as such bears the burden of proof with respect to this motion. 37 CFR §1.633(a). Lederman, however, has failed to demonstrate that Noelle's claims lack of enablement as of November 1, 1996. As such, Lederman Preliminary Motion 4 is ***denied***.

e. ~~Lederman Preliminary Motion 5~~

Lederman Preliminary Motion 4 requests judgement against Noelle claims 51, 56 and 59 on the grounds that they are unpatentable to Noelle under 35 U.S.C. §112, second paragraph. (Lederman Preliminary Motion 5, Paper No. 37, p. 2). According to Lederman, the term "CD40CR" renders claims 51, 56 and 59 "fatally indefinite." (Paper No. 37, p. 7).

The proper standard for definiteness under 35 U.S.C. § 112, second paragraph, is whether a claim reasonably apprises those of skill in the art of its scope. Specifically, when the claims are read in light of the specification, we look to see whether those skilled in the art could understand what is claimed. See *In re Warmerdam*, 33 F.3d 1354, 1361, 31 USPQ2d 1754, 1759 (Fed. Cir. 1994); *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1217, 18 USPQ2d 1016, 1030 (Fed. Cir. 1991). If the scope of the invention sought to be patented cannot be determined from the language of the claims, the specification or the teachings of the prior art with a

reasonable degree of certainty, a rejection of the claims under 35 U.S.C. § 112, second paragraph is appropriate. *In re Wiggins*, 488 F.2d 538, 179 USPQ 421 (CCPA 1973).

Lederman is the moving party for Lederman Preliminary Motion 5, and as such bears the burden of proof with respect to this motion. 37 CFR §1.633(a). Lederman Preliminary Motion 5 fails to meet its burden. Specifically, Lederman has failed to convincingly demonstrate that one skilled in the art could not ascertain whether or not a specific antigen was a CD40CR antigen, i.e., any CD40CR that binds CD40 on any B cell.

Lederman contends that the term CD40CR is indefinite as it is used in Noelle claim 51 and claims 56 and 59, by reason of their dependency on claim 51. (Paper No. 37, pages 7-8). According to Lederman, a person skilled in the art could not ascertain the meaning of CD40CR from the '480 application. In particular, Lederman argues that Noelle's '480 application allows the term CD40CR to encompass any CD40CR that binds CD40 on any B cell, a genus that is "potentially huge." (Paper No. 37, p. 9). Yet, the fact that such a definition of CD40CR is a potentially huge genus does not necessitate a finding that the term is indefinite. Moreover, Lederman has failed to demonstrate that one skilled in the art could not reasonably ascertain whether or not a particular antigen was a CD40CR.

f. Lederman Preliminary Motion 6

Lederman Preliminary Motion 6 requests that the interfering subject matter be redefined. (Lederman Preliminary Motion 6, Paper No. 38, p. 2). Specifically, Lederman Preliminary Motion 6 requests that proposed Counts L-2 and L-3 replace Count 1, the sole count in interference.

Lederman proposed Count L-2 reads as follows:

> A monoclonal antibody which specifically binds and forms a complex with the 5c8 antigen located on the surface of activated T cells and thereby inhibits T cell activation of B cells, the 5c8 antigen being an antigen to which monoclonal antibody 5c8 (ATCC Accession No. HB 10916) specifically binds.
>
> OR
>
> A monoclonal antibody or fragment thereof which specifically binds CD40CR, wherein said CD40CR is expressed by activated human T cells.

(Paper No. 38, p. 9). According to Lederman, claims 1-7 and 10-13 of the Lederman '771 patent and Claims 52 and 60 of Noelle '480 correspond to proposed Count L-2. (Paper No. 38, p. 10).

Lederman proposed Count L-3 reads as follows:

> A monoclonal antibody or fragment thereof which specifically binds to an antigen expressed on activated T cells, wherein said antigen is specifically bound by the monoclonal antibody secreted by hybridoma MR1 which hybridoma has been deposited and accorded ATCC Accession No. HB 11048.

(Paper No. 38, p. 10). According to Lederman, claims 42-43, 46-48, 50, 53-54 and 57 of the Noelle '480 application and no claims of Lederman '771 correspond to proposed Count L-3. (Paper No. 38, pages 10-11).

As stated above, Lederman Preliminary Motion 6 is contingent on the grant, in whole or in part, of any one of Lederman Preliminary Motions 1-5. (Paper No. 38, p. 2). Lederman Preliminary Motions 3, 4 and 5 have been ***denied*** while Lederman Preliminary Motions 1 and 2 have been ***deferred***. To the extent Lederman Preliminary Motion 6 is contingent upon the granting of Lederman Preliminary Motions 1 and 2, Lederman Preliminary Motion 6 is ***deferred***.

g. Lederman Preliminary Motion 7

Lederman Preliminary Motion 7 requests that the interfering subject matter be redefined. (Lederman Preliminary Motion 7, Paper No. 39, p. 2). Specifically, Lederman Preliminary Motion 7 requests that proposed Counts L-2 and L-3 replace Count 1, the sole count in interference.

Lederman proposed Count L-2 reads as follows:

> A monoclonal antibody which specifically binds and forms a complex with the 5c8 antigen located on the surface of activated T cells and thereby inhibits T cell activation of B cells, the 5c8 antigen being an antigen to which monoclonal antibody 5c8 (ATCC Accession No. HB 10916) specifically binds.

(Paper No. 39, p. 9). According to Lederman, claims 1-7 and 10-13 of the Lederman '771 patent correspond to proposed Count L-2. Lederman states that, assuming that Noelle claims 51-52, 56 and 59-60 are patentable to Noelle, no claim of Noelle '480 would correspond to proposed count L-2. (Paper No. 39, p. 10).

Lederman proposed Count L-3 reads as follows:

> A monoclonal antibody or fragment thereof which specifically binds to an antigen expressed on activated T cells, wherein said antigen is specifically bound by the monoclonal antibody secreted by hybridoma MR1 which hybridoma has been deposited and accorded ATCC Accession No. HB 11048.

(Paper No. 39, p. 9). Lederman states that claims 42-43, 46-48, 50, 53-54 and 57 of the Noelle '480 application and none of the Lederman '771 claims correspond to proposed Count L-3. (Paper No. 39, p. 10).

Lederman Preliminary Motion 7 is contingent on the grant, in whole or in part, of any one of Lederman Preliminary Motions 1-5. (Paper No. 39, p. 2). Lederman Preliminary Motions 3, 4 and 5 have been ***denied*** while Lederman Preliminary Motions 1 and 2 have been ***deferred***. To

the extent Lederman Preliminary Motion 7 is contingent upon the granting of Lederman Preliminary Motions 1 and 2, Lederman Preliminary Motion 7 is ***deferred***.

2. Noelle's Preliminary Motions

a. Noelle Preliminary Motions 1

Noelle Preliminary Motion 1 requests that the interfering subject matter be redefined by substituting proposed Count N-2 for Count 1. (Noelle Preliminary Motion 1, Paper No. 46, p. 1). Proposed Count N-2 is identical to Count 1, except that the third part of the count is deleted. (Paper No. 46, p. 3). According to Noelle, Lederman '771 claims 1-7 and 10-13 and Noelle claims 42-43, 46-48, 50, 53-54 and 57 correspond to proposed Count N-2. (Paper No. 46, p. 1).

This motion is said to be contingent upon a determination that Noelle claims 51-53 and 59-60 are unpatentable to Noelle. (Paper No. 46, p. 1). Lederman Preliminary Motion 1 involves a determination of whether Armitage '974 anticipates Noelle claims 51-53 and 59-60. Lederman Preliminary Motion 2 involves a determination of whether Lederman '771 anticipates Noelle claims 51-52 and 59. Both Lederman Preliminary Motion 1 and 2 have been deferred. To the extent Noelle Preliminary Motion 1 is contingent upon Lederman Preliminary Motions 1 and 2, Noelle Preliminary Motion 1 is ***deferred***.

b. Nolle Preliminary Motion 3

Noelle Preliminary Motion 3 requests that the interfering subject matter be redefined by substituting proposed Count N-3 for Count 1. (Noelle Preliminary Motion 3, Paper No. 48, p. 1). According to Noelle, proposed Count N-3 is identical to Count 1, with the exception that the

second part of the current Count is deleted, i.e., the "mouse" part of Count 1 is removed. (Paper No. 48, p. 3). According to Noelle, Lederman '771 claims 1-7 and 10-13 and Noelle claims 52, 53, 59 and 60 would correspond to proposed Count N-2. (Paper No. 48, pages 10 and 11).

This motion is said to be contingent upon a determination that the panel agrees with Lederman that the first and second parts of the Count are directed to separately patentable inventions. (Paper No. 48, p. 7). Lederman Preliminary Motions 6 and 7 seek to redefine the Count and have been deferred. As such, as the relief requested in Noelle Preliminary Motion 3 is contingent upon our grant or denial of Lederman Preliminary Motions 6 and 7, Noelle Preliminary Motion 3 is ***deferred***.

c. Noelle Preliminary Motions 2 and 4

Noelle Preliminary Motions 2 and 4 request priority benefit of the Noelle '799 application and its filing date of February 14, 1992. Noelle Preliminary Motions 2 and 4 are contingent upon the granting of Noelle Preliminary Motions 1 and 3, respectively. As Noelle Preliminary Motions 1 and 3 have been deferred, Noelle Preliminary Motions 2 and 4 are likewise **deferred**.

III. Order

Upon consideration of the record, and for the reasons given, it is:

ORDERED that Lederman Preliminary Motion 1 is ***deferred***.

FURTHER ORDERED that Lederman Preliminary Motion 2 is ***deferred***.

FURTHER ORDERED that Lederman Preliminary Motion 3 is ***denied***.

FURTHER ORDERED that Lederman Preliminary Motion 4 is ***denied***.

FURTHER ORDERED that Lederman Preliminary Motion 5 is ***denied***.

FURTHER ORDERED that Lederman Preliminary Motion 6 is ***deferred***.

FURTHER ORDERED that Lederman Preliminary Motion 7 is ***deferred***.

FURTHER ORDERED that Noelle Preliminary Motion 1 is ***deferred***.

FURTHER ORDERED that Noelle Preliminary Motion 2 is ***deferred***.

FURTHER ORDERED that Noelle Preliminary Motion 3 is ***deferred***.

FURTHER ORDERED that Noelle Preliminary Motion 4 is ***deferred***.

RICHARD TORCZON)
Administrative Patent Judge)
)
)
)
)
SALLY GARDNER-LANE)
Administrative Patent Judge)
)
)
MICHAEL P. TIERNEY)
Administrative Patent Judge)

BOARD OF PATENT
APPEALS
AND
INTERFERENCES

cc: (via Federal Express)

Counsel for Noelle:

R. Danny Huntington,
Robin L. Teskin
BURNS, DOANE, SWECKER & MATHIS
PO BOX 1404
Alexandria VA 22313-1404
Tel.: (703) 836-6620
Fax : (703) 836-2021

Hand Delivery:
1737 King Street
4th Floor
Alexandria, Virginia 22314

Counsel for Lederman:

James F. Haley, Jr.
Margaret A. Pierri
Jane T. Gunnison
Stanley D. Liang
FISH & NEAVE
1251 Avenue of the Americas, 50th Floor
New York, New York 10020
Tel: (212) 596-9000
Fax: (212) 596-9090

INTERFERENCE 104,415
NOELLE V. LEDERMAN
DECISION ON PRELIMINARY MOTIONS

APPENDIX I

CORRELATION OF LEDERMAN'S PRELIMINARY MOTIONS TO NOELLE'S CLAIMS

NOELLE CLAIM #	LEDERMAN'S PRELIMINARY MOTIONS				
	MOTION 1 102(e), Armitage	MOTION 2 102(e), Lederman	MOTION 3 112, 1st, Description	MOTION 4 112, 1st, Enablement	MOTION 5 112, 2nd, Indefiniteness
42	✔				
43	✔				
45					
46	✔				
47	✔			✔	
48				✔	
50				✔	
51	✔	✔	✔	✔	✔
52	✔	✔	✔	✔	
53	✔		✔	✔	
54				✔	
55					
56		✔	✔	✔	✔
57	✔				
59	✔	✔	✔	✔	✔
60	✔	✔	✔	✔	

Paper 109

Ruled by: Michael P. Tierney
Administrative Patent Judge
Box Interference
Washington, D.C. 20231
Tel: 703-308-9797
Fax: 703-305-0942

Filed
June 28, 2001

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

RANDOLPH NOELLE
(08/742,480)

Junior Party

SETH LEDERMAN, LEONARD CHESS
and MICHAEL J. YELLIN
(5,474,771)

Senior Party

Patent Interference No. 104,415

MAILED

JUN 29 2001

PAT. & T.M. OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

TIERNEY, Administrative Patent Judge

ORDER

(Rejection Under 37 CFR 1.641 and Order to Show Cause)

The involved Noelle 08/742,480 application ("'480 application") was filed on November 1, 1996. Noelle '480 is said to be a continuation of U.S. Application No. 08/328,975 ("'975 application"), filed November 14, 1994, which itself is said to be a continuation of U.S.

Application No. 07/835,799 ('799 application), filed February 14, 1992. (Lederman Preliminary Motion 1, Paper No. 33, p. 3).

The Board has determined that Noelle claims 51, 52, 53, 56, 59 and 60 are not entitled to 35 U.S.C. §120 benefit of the Noelle '799 filing date of February 14, 1992. (Memorandum Opinion and Order, Paper No. 108). Accordingly, the earliest possible effective filing date for these claims is the November 14, 1994 filing date of the Noelle '975 application. Lacking §120 benefit of the February 14, 1992 filing date, the Administrative Patent Judge has become aware of reasons why Noelle's claims 51, 52, 53, 56, 59 and 60 may not be patentable.

I. Rejections Under 37 CFR §1.641

A review of the record indicates that there are numerous publications and references that, while not available as prior art against Noelle's '799 February 14, 1992 filing date, are available under 35 U.S.C. §102(b) against Noelle's '975 filing date of November 14, 1994. For instance:

i. Seth Lederman et al., *Identification of a Novel Surface Protein on Activated CD4$^+$ T Cells That Induces Contact-dependent B Cell Differentiation (Help)*, 175 J. Exp. Med. 1091-1101 (April 1992). (LX 1029).

ii. Melanie K. Spriggs et al., *Recombinant Human CD40 Ligand Stimulates B Cell Proliferation and Immunoglobulin E Secretion*, 176 J. Exp. Med. 1543-1550, (December 1992). (LX 1032).

iii. Randolph J. Noelle et al., *CD40 and its ligand, an essential ligand-receptor pair for thymus-dependent B-cell activation*, Vol. 13, No. 11, Immunology Today 431-433, (1992). (LX 1048).

iv. Diane Hollenbaugh et al., *The human T cell antigen gp39, a member of the TNF gene family, is a ligand for the CD40 receptor, expression of a soluble form of gp39 with a B cell co-stimulatory activity*, Vol. 11, No. 12, EMBO Journal 4313-4321, (December 1992). (LX 1082).

Additionally, both the Lederman '771 patent and the Armitage '974 patent were listed as priority documents in international applications. Specifically, the Armitage 07/783,707 and 07/805,723 applications, which are the parent applications of the Armitage 08/249,189 application that issued as Armitage '974, are listed as priority applications for Armitage WO 93/08207. Similarly, the Lederman 07/792,728 application, which issued as Lederman '771, is listed as the priority application for Lederman WO 93/09812. Both the Armitage WO 93/08207 and Lederman WO 93/09812 publications are 35 U.S.C. §102(b) prior art to Noelle claims 51, 52, 53, 56, 59 and 60 due to their respective publication dates of April 29, 1993 and May 27, 1993.

To simplify the issues presented in the §641 rejections, the parties attention is directed to the teachings contained in the prior art Lederman WO 93/09812 and Armitage WO 93/08207 publications.

A. Noelle Claims 51, 52, 56, 59 and 60 are Rejected Under 35 U.S.C. §102(b) as Anticipated by Lederman WO 93/09812.

Noelle claims 51, 52, 56, 59 and 60 are rejected under 35 U.S.C. §102(b) as anticipated by Lederman WO 93/09812, a copy of which is attached to this Order.

Lederman WO 93/09812 claims priority to U.S. Application 792,728 filed on November 15, 1991. The U.S. '728 application issued as Lederman '771 on December 12, 1995. For the purposes of this rejection, the Lederman '771 patent and Lederman WO 93/09812 publication contain the same basic description of a human CD40 counter receptor ("5c8," "CD40CR") and an antibody that is specific to that human CD40CR.

Lederman Preliminary Motion 2 requests judgment against Noelle claims 51, 52, 56, 59 and 60 on the grounds that they are anticipated under 35 U.S.C. §102(e) by Lederman '771. (Lederman Preliminary Motion 2, Paper No. 34, p. 2). In responding to Lederman Preliminary Motion 2, Noelle did not dispute Lederman's assertion that Lederman '771 described and enabled the subject matter of Noelle claims 51, 52, 56, 59 and 60. (Noelle Opposition 2, Paper No. 58, admission of Lederman facts 12, 14, 15, 16, 17, 18 and 19). Rather than distinguish Noelle's claims from the teachings of the '771 patent, Noelle Opposition 2 states that Noelle has a date of invention prior to the effective date of the '771 patent, and thus, the '771 patent would not be prior art to Noelle. (Paper No. 58, page 4). Moreover, at the April 12, 2001 hearing, Noelle's counsel confirmed that, with respect to Lederman Preliminary Motions 1 and 2, Noelle did not "have a case other than an antedating case." (April 12, 2001, Hearing Transcript, p. 78, line 21 to p. 79, line 22). Yet, as Lederman WO 93/09812 is anticipatory prior art under 35 U.S.C. §102(b), Noelle cannot antedate the Lederman WO 93/09812 publication. Accordingly, Noelle claims 51, 52, 56, 59 and 60 are unpatentable to Noelle as they are anticipated under 35 U.S.C. §102(b) by Lederman WO 93/09812.

A claim-by-claim comparison of Lederman WO 93/09812 publication and Noelle claims 51, 52, 56, 59 and 60 is provided below.[1]

[1]Additionally, the parties are directed to the statements contained in Lederman Preliminary Motion 2 and its attached Appendix 1.

Noelle Claim 51

A monoclonal antibody or fragment thereof which specifically binds CD40CR

Lederman WO 93/09812 describes and enables a monoclonal antibody 5c8 that specifically binds 5c8 antigen (human CD40CR antigen).[2] (Page 53, line 16 to page 55, line 11). As the monoclonal antibody 5c8 falls within Noelle's claimed genus of monoclonal antibodies that bind a CD40CR, Lederman WO 93/09812 anticipates Noelle claim 51.

Noelle Claim 52

The monoclonal antibody or fragment of Claim 51, wherein said CD40CR is expressed by activated human T cells.

In addition to describing the monoclonal antibody 5c8, Lederman WO 93/09812 describes and enables an isolated protein, 5c8 antigen, that is expressed on the surface of activated human T cells. (Page 6, lines 13-16; page 22, lines 14-17; page 65, line 25 to page 67, line 16). Accordingly, Lederman WO 93/09812 anticipates Noelle claim 52.

---

[2]CD40CR is the antigen in Lederman's '771 patent and Noelle's '480 application. The antigen CD40CR is referred to as "T-B cell activating molecule" by Lederman '771, as "glycoprotein 39" by Noelle '480, and "CD40 ligand" (CD40L) by Armitage U.S. Patent No. 5,961,974 (Armitage '974). (Kelsoe Declaration, ¶ 9, LX 1006). In particular, Lederman '771 uses the term 5c8 antigen to describe ***human*** CD40CR. Similarly, Noelle uses the term gp39 to describe ***mouse*** CD40CR antigen. (Kelsoe Declaration, ¶ 9 and 15, LX 1006).

Noelle Claim 56

A pharmaceutical or diagnostic composition containing a pharmaceutically or diagnostically effective amount of the monoclonal antibody according to Claim 51 and a pharmaceutical or diagnostically acceptable carrier.

Lederman WO 93/09812 describes and enables the monoclonal antibody 5c8. Moreover, Lederman WO 93/09812 describes and enables a pharmaceutical composition comprising the 5c8 monoclonal antibody and a pharmaceutically acceptable carrier. (Page 18, lines 10-21). In particular, Lederman WO 93/09812 describes administering an effective inhibiting amount of a pharmaceutical composition comprising the monoclonal antibody which specifically recognizes the activated T cell surface protein and a pharmaceutically acceptable carrier. (Page 27, lines 13-19). Accordingly, Noelle claim 56 is anticipated by Lederman WO 93/09812.

Noelle Claim 59

A cell line which produces an antibody according to Claim 51.

Lederman WO 93/09812 describes and enables a hybridoma cell having ATCC Accession No. HB 10916 that produces the monoclonal antibody 5c8. (Page 17, lines 16-31). Accordingly, Lederman WO 93/09812 anticipates Noelle claim 59.

Noelle Claim 60

A cell line which produces an antibody according to Claim 52.

Lederman WO 93/09812 describes and enables a hybridoma cell having ATCC Accession No. HB 10916 that produces the monoclonal antibody 5c8. (Page 17, lines 16-31). Accordingly, Lederman WO 93/09812 anticipates Noelle claim 59.

B. Noelle Claims 51, 52, 53, 59 and 60 are Rejected Under 35 U.S.C. §102(b) as Anticipated by Armitage WO 93/08207.

Noelle claims 51, 52, 53, 59 and 60 are rejected under 35 U.S.C. §102(b) as anticipated by Armitage WO 93/08207, a copy of which is attached to this Order.

Armitage WO 93/08207 claims priority to U.S. applications 07/783,707 and 07/805,723. The Armitage 08/249,189 application that issued as Armitage '974, also claims benefit of the 07/783,707 and 07/805,723 applications. For the purposes of this rejection, the Armitage '974 patent and Armitage WO 93/08207 publication contain the same basic description of a human CD40 counter receptor ("CD40CR") and an antibody that is specific to that human CD4CR as well as a mouse CD40CR and an antibody that is specific to mouse CD40CR.

Lederman Preliminary Motion 1, *inter alia*, requests judgment against Noelle claims 51-52, 53, 59 and 60 on the grounds that they are anticipated under 35 U.S.C. 102(e) by Armitage '974. (Lederman Preliminary Motion 1, Paper No. 33, p. 2). In its Opposition to Lederman Preliminary Motion 1, Noelle did not dispute Lederman's assertion that Armitage '974 described and enabled the subject matter of Noelle claims 51, 52, 53, 59 and 60. (Noelle Opposition 1, Paper No. 57, admission of Lederman facts 15 and 18). Rather than distinguish Noelle's claims from the teachings of the '974 patent, Noelle Opposition 1 states that Noelle has a date of invention prior to the effective date of the '974 patent, and thus, the '974 patent would not be prior art to Noelle. (Paper No. 57, page 4). Moreover, at the April 12, 2001 hearing, Noelle's counsel confirmed that, with respect to Lederman Preliminary Motions 1 and 2, Noelle did not "have a case other than an antedating case." (April 12, 2001, Hearing Transcript, p. 78, line 21 to p. 79, line 22). Yet, as Armitage WO 93/08207 is anticipatory prior art under 35 U.S.C.

Noelle cannot antedate the Armitage WO 93/08207 publication. Accordingly, Noelle claims 51, 52, 53, 59 and 60 are unpatentable to Noelle as they are anticipated under 35 U.S.C. §102(b) by Armitage WO 93/08207.

A claim-by-claim comparison of Armitage WO 93/08207 publication and Noelle claims 51, 52, 53, 59 and 60 is provided below.[3]

Noelle Claim 51

A monoclonal antibody or fragment thereof which specifically binds CD40CR

Armitage WO 93/08207 describes and enables the isolation human CD40 ligand, i.e., human CD40CR and the generation of monoclonal antibodies that specifically bind human CD40 ligand. (Abstract, page 5, lines 21-24, Examples 1 and 7). The nucleotide and amino acid sequence corresponding to the human CD40-L are also described. (SEQ ID No. 11, No. 12 and Figure 2). Accordingly, Armitage WO 93/08207 anticipates Noelle claim 51.

Noelle Claim 52

The monoclonal antibody or fragment of Claim 51, wherein said CD40CR is expressed by activated human T cells.

As discussed above, Armitage WO 93/08207 describes and enables the isolation human CD40 ligand, i.e., human CD40CR and the generation of monoclonal antibodies that specifically bind human CD40 ligand. Armitage's human CD40CR nucleotide and amino acid sequence was

[3]Additionally, the parties are directed to the statements contained in Lederman Preliminary Motion 1 and its attached Appendix 1.

found by using activated human peripheral blood lymphocytes. (Page 19, lines 15-36). As such, Armitage WO 93/08207 anticipates Noelle claim 52.

Noelle Claim 53

The monoclonal antibody or fragment of Claim 51, wherein said CD40CR is expressed by activated murine T cells.

The term "murine" includes rats and mice. (Paper No. 57, admission of Lederman fact 19). Armitage WO 93/08207 describes and enables isolated mouse CD40CR antigens. (Abstract, p. 5 lines 21-23). Additionally, Armitage WO 93/08207 describes and enables the generation of monoclonal antibodies to purified mouse CD40CR. (Example 7).

A person skilled in the art would appreciate that mouse helper T cells activate mouse B cells. That person would have also appreciated that Armitage's mouse CD40CR antigen would inherently be expressed by mouse activated T cells. (Declaration of Ethan M. Shevach, M.D., LX 1007, ¶ 14). Accordingly, Armitage WO 93/08207 anticipates Noelle claim 53.

Noelle Claim 59

A cell line which produces an antibody according to Claim 51.

Armitage WO 93/08207 describes and enables the production of monoclonal antibodies to CD40CR using hybridoma cells. (Example 7). Furthermore, Armitage WO 93/08207 specifically describes the preparation of monoclonal antibodies to human CD40CR using hybridoma cells. (Example 7). Accordingly, Armitage WO 93/08207 anticipates Noelle claim 59.

Noelle Claim 60

A cell line which produces an antibody according to Claim 52.

Armitage WO 93/08207 describes and enables the production of monoclonal antibodies to CD40CR using hybridoma cells. (Example 7). Furthermore, Armitage WO 93/08207 specifically describes the preparation of monoclonal antibodies to human CD40CR using hybridoma cells. (Example 7). Accordingly, Armitage WO 93/08207 anticipates Noelle claim 60.

II. Question of No Interference-in-Fact

As noted at the Oral Hearing of April 12, 2001, and in Noelle Oppositions 6 and 7, Lederman Preliminary Motions 6 and 7 seek the wrong relief. Specifically, Lederman Preliminary Motions 6 and 7 proposed counts for which Lederman would have no corresponding claims. (Noelle Oppositions 6 and 7, Papers 62 and 63, p. 13). As apparent from the motions and as noted at the oral hearing, for all practical purposes Lederman Preliminary Motions 6 and 7 request a finding of no interference-in-fact.[4]

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[4]See the transcript of the April 12, 2001 oral hearing page 26, line 13 to page 28, line 21. For example:

> Judge Torczon: For formal reasons, do we even need the mouse count [of Lederman Preliminary Motions 6 and 7]? If they're separate inventions does Lederman have any claims - -
>
> Mr. Haley: We do not need the mouse count. And the reason there is no interference-in-fact motion is because Noelle has a generic claim, and hence, that generic claim would correspond to either human or mouse. As we understood the rules under that situation, there could be no interference-in-fact motion.

(April 12, 2001 Transcript, p. 26, line 22 to page 27, line 11).

Lederman Preliminary Motion 6 raised the question of whether or not an interference-in-fact exists between Noelle's claims and Lederman's claims if Noelle claims 51, 56 and are unpatentable to Noelle. (Paper No. 38 and Paper No. 39). Similarly, Lederman Preliminary Motion 7 raised the question of whether or not an interference-in-fact exists between Noelle's claims and Lederman's claims if Noelle claims 51, 52, 56, 59 and 60 are unpatentable to Noelle. Specifically, both Lederman Preliminary Motions 6 and 7 raised the question of whether Lederman's claimed anti-human CD40CR antigen monoclonal antibodies are novel and unobvious in view of Noelle's claimed anti-mouse CD40CR antigen monoclonal antibodies. Lederman's Preliminary Motions 6 and 7 were opposed on the merits by Noelle in Noelle Oppositions 6 and 7.

Lederman Preliminary Motions 6 and 7 are contingent motions that are said to be contingent on the grant, in whole or in part, of any one of Lederman Preliminary Motions 1-5. (Paper No. 38, p. 2). Lederman Preliminary Motions 1 and 2 generally involve rejections of Noelle claims 51, 52, 53, 56, 59 and 60 under 35 U.S.C. §102(e) based upon Armitage '974 and/or Lederman '771. Lederman Preliminary Motions 1 and 2 have been *deferred* and based on this deferral, Lederman Preliminary Motions 6 and 7 were likewise *deferred*. The above 35 U.S.C. §102(b) rejections, however, involve patentability questions similar to those presented in Lederman Preliminary Motions 1 and 2. Accordingly, if the §102(b) rejections are maintained, the question of no interference-in-fact raised in Lederman Preliminary Motions 6 and 7 would be ripe for consideration.

Noelle Preliminary Motions 1 and 3 are contingent motions that seek to redefine the interfering subject matter. Specifically, Noelle Preliminary Motion 1 is contingent upon a

determination that Noelle claims 51-53 and 59-60 are unpatentable to Noelle. (Paper No. 46, p. 1). Additionally, Noelle Preliminary Motion 3 is said to be contingent upon a determination that the panel agrees with Lederman that the first and second parts of the Count are directed to separately patentable inventions. (Paper No. 48, p. 7). Lederman Preliminary Motions 6 and 7 seek to redefine the Count and have been *deferred*. Based on this deferral, Noelle Preliminary Motions 1 and 3 were also *deferred*. Similarly, as Noelle Preliminary Motions 2 and 4 requested priority benefit of the Noelle '799 application and were contingent upon Noelle Preliminary Motions 1 and 3, Noelle Preliminary Motions 2 and 4 were *deferred*. If the §102(b) rejections are maintained, the question of no interference-in-fact raised in Lederman Preliminary Motions 6 and 7 would be ripe for consideration, and consequently, Noelle Preliminary Motions 1-4 would also be ripe for consideration.

III. Order to Show Cause

Noelle is ordered to show cause why, in light of the above §102(b) rejections over Lederman '771 and Armitage '974, Noelle claims 51, 52, 53, 56, 59 and 60 are patentable to Noelle. Pursuant to 37 CFR 1.641(a) the following times are set for response. The parties have until **July 31, 2001** to file written comments responding to this order. The parties then have until **August 31, 2001** to file a written opposition to any written comments submitted by the opposing party. These times are not subject to extension without prior consultation of an Administrative Patent Judge and a showing of good cause. If after briefing, I decide to maintain the above §102(b) rejections, the parties will proceed to final hearing.

Michael P. Tierney
Administrative Patent Judge

Date: 6/28/01
Arlington, VA

cc: (via Federal Express)

Counsel for Noelle:

R. Danny Huntington,
Robin L. Teskin
BURNS, DOANE, SWECKER & MATHIS
PO BOX 1404
Alexandria VA 22313-1404
Tel.: (703) 836-6620
Fax : (703) 836-2021

Hand Delivery:
1737 King Street
4th Floor
Alexandria, Virginia 22314

~~Counsel for Lederman:~~

James F. Haley, Jr.
Margaret A. Pierri
Jane T. Gunnison
Stanley D. Liang
FISH & NEAVE
1251 Avenue of the Americas, 50th Floor
New York, New York 10020
Tel: (212) 596-9000
Fax: (212) 596-9090

ADDENDUM 3

The opinion in support of the decision being entered today is not binding precedent of the Board.

Paper No. 135

Filed by: Trial Section Motions Panel
Box Interference
Washington, D.C. 20231
Tel: 703-308-9797
Fax: 703-305-0942

Filed: 19 October 2001

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

RANDOLPH NOELLE
(08/742,480),
Junior Party,

v.

SETH LEDERMAN, LEONARD CHESS,
and MICHAEL J. YELLIN
(5,474,771),
Senior Party.

Patent Interference No. 104,415

Before: TORCZON, GARDNER-LANE and TIERNEY, Administrative Patent Judges.

TIERNEY, Administrative Patent Judge.

FINAL DECISION
(Decision on Lederman Preliminary Motion 8)

This interference is before a motions panel for a decision on preliminary motions. Oral argument took place on September 26, 2001. Representing Junior Party Noelle at oral argument was E. Anthony Figg and Robin L. Teskin. Senior Party Lederman was represented by James F. Haley, Jr., Margaret A. Pierri, Jane Gunnison and Stanley D. Liang. A transcript of the oral argument appears in the record. (Paper No. 134).

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I. Summary of the Opinion

This is an interference between Junior Party Noelle (real party in interest, IDEC Pharmaceuticals, Inc.) and Senior Party Lederman (real party in interest, Biogen, Inc.). The sole issue before this panel is the question of whether or not there exists an "interference-in-fact" between Noelle's remaining patentable claims and Lederman's claims. More particularly, there is a dispute as to whether, at the relevant time, a person of ordinary skill in the art having either the anti-mouse or anti-human CD40 counter-receptor antibodies would have had a reasonable expectation of success of obtaining the other.

Noelle has demonstrated that one skilled in the art, given the anti-mouse or anti-human antibodies, would have expected its human or mouse counterpart to exist. Moreover, Noelle has sufficiently demonstrated that screening techniques for antibodies were well known in the art at the relevant date. Nevertheless, Lederman has demonstrated that one skilled in the art, provided with Noelle's "mouse" claims and the prior art, would not have had a reasonable expectation of success of obtaining the anti-human antibodies. Accordingly, we hold that Lederman has sufficiently established that its "human" claims are not obvious or anticipated by Noelle's "mouse" claims. As such, no interference-in-fact exists between Noelle's remaining patentable claims and Lederman's claims.

II. Previous Decisions in the Interference

As set forth in the Memorandum, Opinion and Order ("Memorandum," Paper No. 108), this interference concerns CD40 counter-receptors for the CD40 B-cell antigen and monoclonal

antibodies for these CD40 counter-receptors. CD40 counter-receptors are expressed on activated T cells and are also known as CD40CRs or CD40Ls.

This interference was declared with a single count having three alternative embodiments.[1] To simplify the terminology in this interference, the first alternative can be generally referred to as the "human" antibody to human CD40CR, the second alternative as "mouse" antibody to mouse CD40CR and the third alternative as the "genus" of antibodies to CD40CRs. Noelle's involved application had claims directed to all three alternative embodiments whereas Lederman's involved patent presents claims directed to only the "human" embodiment.

For each of its three claimed embodiments, Noelle sought 35 U.S.C. § 120 benefit of U.S. Application No. 08/338,975, filed November 14, 1994, as well as U.S. Application No. 07/835,799, filed February 14, 1992. During the course of the interference, it was determined that Noelle's "genus" and "human" embodiments lacked written descriptive support in Noelle's '799 application as of the February 14, 1992 filing date. (Paper No. 108, pages 23-33). Lacking benefit of its 1992 filing date, an Administrative Patent Judge became aware of reasons why Noelle's "genus" and "human" claims were unpatentable under 35 U.S.C. § 102(b).

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[1] The interference was declared on September 3, 1999, (Paper No. 1), with Count 1 which reads as follows:

> The monoclonal antibody of claim 1 of 5,474,771 [Lederman] or the monoclonal antibody of claim 42 or claim 51 of 08/742,480 [Noelle].

(Paper No. 1, p. 46). Claim 1 of Lederman '771 is directed to a monoclonal antibody that specifically binds and forms a complex with a 5c8 antigen ("CD40CR")("human" embodiment) whereas claim 42 of Noelle is directed to a monoclonal antibody or fragment thereof which specifically binds a mouse CD40CR ("mouse" embodiment) and Noelle claim 51 is directed to a monoclonal antibody or fragment thereof that specifically binds CD40CR ("genus" embodiment). (See, Paper No. 108, facts 4-7).

Accordingly, the Judge issued an Order under 37 CFR § 1.641 rejecting Noelle's "genus" and "human" claims as anticipated by the disclosures of Lederman WO 93/09812 and/or Armitage WO 93/08207. (Paper No. 109). Although reserving the right to appeal, Noelle did not contest the finding that Noelle's "genus" and "human" claims lacked written descriptive support as of the February 14, 1992 filing date and did not contest the unpatentability of these claims under 35 U.S.C. §102(b). (Lederman Preliminary Motion 8, Paper No. 116, pages 2-3, facts 4, 5, Noelle Opposition 8, Paper No. 118, p. 3, admitted facts 4 and 5).[2]

Lederman Preliminary Motions 6 and 7 sought to redefine the interfering subject matter. As noted during the oral argument of April 12, 2001, Lederman's motions were defective. Specifically, Lederman proposed counts that did not correspond to any of Lederman claims. Yet, as apparent from the motions and as noted at the oral argument of April 12, 2001, for all practical purposes Lederman Preliminary Motions 6 and 7 requested a finding of no interference-in-fact. (Order, Paper No. 109, pages 10-12).

Our Memorandum (Paper No. 108) deferred resolution of Lederman Preliminary Motions 6 and 7 as they were contingent upon Lederman's prior art patentability motions 1 and 2, which were deferred. As we determined that Noelle's "human" and "genus" claims were unpatentable to Noelle, the issue of no interference-in-fact was ripe for consideration. Counsel for both Noelle and Lederman agreed to rebrief the issue of no interference-in-fact. Specifically, times were set

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[2]Lederman filed a revised Lederman Preliminary Motion 8 (Paper No. 116) to correct what it termed "typographical" errors in its originally filed Lederman Preliminary Motion 8 (Paper No. 113). Lederman's revised motion was entered into the record. Accordingly, this opinion refers to the revised Lederman Preliminary Motion 8 (Paper No. 116) as "Lederman Preliminary Motion 8."

for Lederman to withdraw its motions 6 and 7 and to file a new motion, Lederman Preliminary Motion 8, to correct the procedural defects noted in Lederman Preliminary Motions 6 and 7. Likewise, times were set to allow for Noelle to oppose this motion and for Lederman to reply to Noelle's opposition. (Order Setting Times, Paper No. 111, Order Setting Times, Paper No. 117, and Decision on Miscellaneous Motion, Paper No. 127).

In response to Lederman Preliminary Motion 8, Noelle has filed Noelle Opposition 8 (Paper No. 118) which identifies and relies upon exhibits 2084-2095, as well as earlier-filed exhibits. In the Order Setting Times (Paper No. 111) and in the Communication of September 10, 2001 (Paper No. 122), the parties were informed that a party wishing to submit new evidence in this interference was to submit a miscellaneous motion under 37 CFR § 1.635, which was to show good cause as to why the new evidence could not have been previously presented in the interference. Seeking to have the new evidence entered into the record, Noelle filed Noelle Miscellaneous Motion 1 (Paper No. 125) which, *inter alia*, requested: 1) entry of Noelle exhibits NX 2086, 2088, 2089, 2090-2091; and 2) withdrawal of Noelle exhibits NX 2084 and 2092-2095. (Paper No. 125, p. 2). As set forth in the Decision on Miscellaneous Motion (Paper No. 127), Noelle Exhibits NX 2086, 2088, 2090 and 2091 were entered into the record whereas Noelle Exhibits NX 2084, NX 2089 and NX 2092-2095 were ***not*** entered into the record.[3]

[3]Noelle Miscellaneous Motion 1 noted that Noelle Exhibits NX 2085 and 2087 were already in evidence as Lederman Exhibits LX 1052 and 1095, respectively. (Paper No. 125, p. 2).

III. Findings of Fact

A. Previous Findings

We reaffirm our previous findings of fact and conclusions of law made in this interference. As background information on the issue of reasonable expectation of success, we reiterate findings of fact 32, 33, 35 and 36 from our Memorandum, Paper No. 108:

Fact 32. As of February 14, 1992, the isolation and purification of CD40 counter receptors ("CD40CR") was ***not*** a predictable art. As of this date, the skilled artisan could not have predicted with any reasonable degree of certainty from Noelle's disclosure whether particular CD40CRs and the antibodies specific to the CD40CRs could be generated and isolated other than Noelle's disclosed mouse CD40CR and the antibodies specific to the mouse CD40CR. Indeed, it would have been difficult for the skilled artisan to generate and isolate the CD40CRs and antibodies specific to the CD40CRs beyond those disclosed by Noelle's application. (See generally, LX 1006, LX1007, LX 1092 and LX 1093).

Fact 33. As of February 14, 1992, the construction of CD40-Ig fusion protein, such as Noelle's CD40-Ig, would have been extremely difficult. (LX 1092, ¶ 16, LX1093, ¶ 10). During the prosecution history of Noelle's parent U.S. Application No. 07/835,799, Dr. Sandro Aruffo submitted a declaration stating that:

> Prior to the actual construction of the CD40-immunoglobin fusion protein disclosed and claimed in the above-identified patent application [07/835,799], I and my co-inventors could not predict whether this approach would result in a biologically active fusion protein.

(Declaration of Aruffo under 37 C.F.R. 1.132 dated July 7, 1994, LX 1009, p. 2). Dr. Aruffo further stated that:

> [E]ach individual fusion protein must be constructed independently, and whether a particular fusion protein can be successfully generated is often not determinable until the experiment is performed. In view of this lack of predictability, there is not a reasonable expectation of success prior to the actual

> production of a recombinant immunoglobin fusion molecule.

(Declaration of Aruffo under 37 C.F.R. 1.132 dated July 7, 1994, LX 1009, p. 3).

Fact 35. One skilled in the art reviewing the Noelle '480 application would have doubts regarding the validity of Section 7 [which discusses the binding of a CD40Ig fusion protein to human T-cell lines]. Specifically, a control should have been included in Section 7 to confirm that the reported binding is due to the CD40 moiety, rather than the Ig moiety, of the CD40-Ig fusion protein. (LX1007, ¶ 39, LX 1006, ¶ 30). Absent the proper control, one skilled in the art could not have known whether the CD40-Ig fusion protein was binding to a cell surface protein on Jurkat and HSB2 cells via the CD40 portion of the CD40-Ig molecule. (LX1007, ¶ 39, LX 1006, ¶ 30). At best, Noelle's expert, Dr. Clark, states that:

> In my opinion, ***it is more plausible than not to assume that the results in Section 7 and Figure 7 are valid***, e.g., attributable to the CD40 portion of the fusion protein as the Noelle application describes several other experiments (described in Section 6.2.3 of Noelle Application), wherein an appropriate control, i.e., CD7E-Ig was utilized and confirmed that the observed binding of the CD40-Ig to activated mouse T helper cells and CD40, and not the Ig moiety of the fusion protein.

(NX 2012, ¶ 14, emphasis added).

Fact 36. As of February 14, 1992, it would have been difficult for one of ***ordinary*** skill in the art to conduct the expression cloning methodology recited in the Noelle '480 application. (Amendment and Response filed October 1, 1993 in support of Armitage, U.S. Application No. 07/969,703, LX 1083, p. 7, LX 1092, ¶ 45 on p. 17, LX 1093, ¶ 33).

B. Additional Findings

We make the following additional findings of fact:

37. The claims of the parties are as follows:

(i) The claims of the parties were:

Noelle '480 :	42, 43, 45-48, 50-57, 59 and 60[4]
Lederman '771:	1-14

(ii) The claims of the parties which corresponded to Count 1 were:

Noelle '480 :	42, 43, 46-48, 50-54, 56, 57, 59 and 60
Lederman '771:	1-7 and 10-13

(iii) The claims of the parties which did not correspond to Count 1 are:

Noelle '480 :	45 and 55
Lederman '771:	8, 9 and 14

(Paper No. 1, p. 46). Noelle claims 51, 52, 53, 56, 59 and 60 are directed to the "genus" and "human" embodiment of Count 1. These claims have been determined unpatentable to Noelle. Accordingly, Noelle's corresponding claims are 42, 43, 46-48, 50, 54, and 57.

38. At the relevant time, one skilled in the art believed that the induction of B lymphocyte responses was a complex process. Specifically, one skilled in the art believed:

> The induction of B lymphocyte responses is a complex process that is initiated and regulated by T lymphocytes. T cells effect B cell responses via direct cell-cell contact or by means of soluble cytokines. Although early studies focused on the role of surface Ig in the activation of B cells, more recent studies have suggested that surface Ig facilitates the capacity of B cells to take up specific Ag and present it to T cells in a MHC-restricted manner, but may not otherwise be involved in T cell-B cell collaboration. ***The precise mechanisms by which T cells stimulate B cells remains unclear.***

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[4]Noelle originally cited claim 58 as a pending claim. (Noelle's Clean Copy of Pending Claims, Paper No. 7). Claim 58, however, was cancelled by Examiner's Amendment during the prosecution of the '480 application. (Noelle Clarification of Status of Claim 58, Paper No. 45, '480 Prosecution History, Examiner's Amendment, Paper No. 10, mailed August 12, 1998).

(LX 1095, p. 2544, right col., lines 8-18, emphasis added).

39. At the relevant time, one skilled in the art understood that:

> [A] variety of receptor ligand interactions appeared to be involved in the collaboration with activated T cells inducing B cell proliferation and differentiation.

(LX 1095, p. 2545, left col., lines 7-10).

40. Prior to the earliest application filing dates of Lederman and Noelle, it was known that both human and mouse B cells expressed CD40, an antigen involved in B cell differentiation. (LX 1079, p. 35, last ¶, Paper No. 118, p. 5, fact 32, Paper No. 129, p. 1, admitting fact 32).

41. In April 1991, i.e., prior to the earliest application filing dates of both Lederman and Noelle, Lederman published an abstract (Lederman et al., Clin. Res. 39(2):380A, April 1991, NX 2086) regarding the mechanism of inducing B cell differentiation by a CD4- Jurkat clone, identified as Jurkat clone (D1.1). This abstract "suggested" that molecular features on the D1.1 human T cell line, other than a lack of CD4, accounted for a constitutive ability to induce B cell activation. (NX 2086, page 380A, last line).

42. At the relevant time, the known existence of the mouse CD40CR and the general conservation in function of immune cell molecules across species would have suggested the existence of the corresponding human CD40CR. (See generally, NX 2012, ¶¶ 17, 18).

43. One skilled in the art studying B cell responses, at the relevant time, would have found it difficult to extrapolate the results obtained from anti-mouse CD40CR antibodies to anti-human CD40CR antibodies. Specifically:

> [D]ifferences between the regulation of human and murine B cells make it additionally difficult to extrapolate the results obtained from one system to another.

(LX 1095, p. 2544, right col., lines 39-42).

44. Immunization with activated human T cells or activated or non-activated cell lines, such as Jurkat and HSB2, would raise a number of known and unknown T cell proteins such as CD4, OX40 receptor, CD25, MHC class II and ICAM-1. (LX 1093, Second Kelsoe Declaration, ¶ 26).

IV. Lederman Preliminary Motion 8

Lederman Preliminary Motion 8 moves for judgment, and termination of this interference on the grounds that there is no interference-in-fact between Lederman's "human" claims and Noelle's "mouse" claims. (Lederman Preliminary Motion 8, Paper No. 116, p. 1). Noelle opposes this motion.

A. No Interference-In-Fact is a One-Way Distinctiveness Test

The question of whether there is no interference-in-fact is a one-way distinctiveness test. Specifically, a movant can establish that no interference-in-fact exists by showing that its claimed

invention is patentably distinct from the opponents claimed invention. See Example 20[5], Notice of Final Rule, Patent Interference Proceedings, 49 Fed. Reg. 48416, 48424 (col. 1) (Dec. 12, 1984). Thus, for Lederman to succeed in its motion for no interference-in-fact, Lederman need only demonstrate that: (i) Lederman's claims are not anticipated or rendered obvious by Noelle's remaining "mouse" claims; ***or*** (ii) Noelle's remaining "mouse" claims are not anticipated or rendered obvious by Lederman's claims.

1. Anticipation is Not an Issue in this Interference

Both Noelle and Lederman agree that their corresponding claims, read in light of the prior art, do not anticipate each others claims. (Noelle Opposition 8, Paper No. 118, p. 21, Lederman Reply 8, Paper No. 129, p. 4).

2. Obviousness Requires Both Motivation and Reasonable Expectation of Success

As to obviousness, both parties agree that a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (i) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed subject matter; and (ii) whether the

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[5]Example 20. Application AD contains patentable claim 1 (6-cylinder engine). Application AE contains patentable claim 3 (8-cylinder engine). An interference is declared with a single count (6 or 8-cylinder engine). Claim 1 of application AD and claim 3 of application AE are designated to correspond to the count. Applicant AD believes that a 6-cylinder engine is a "separate patentable invention" (See § 1.601(n)) from an 8-cylinder engine. Applicant AD would file a motion under § 1.633(b) for judgment on the ground of no interference-in-fact stating why a 6-cylinder engine is patentably distinct from an 8-cylinder engine. If the Board ultimately agrees with Applicant AD, a patent could issue to AD containing claim 1 of application AD and a second patent could issue to AE containing claim 3 of application AE.

prior art would also have revealed that in making the claimed subject matter, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chem.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

a. Motivation is Not an Issue in this Interference

The parties agree that, at the relevant date, the skilled worker having anti-human CD40CR antibodies or anti-mouse CD40CR antibodies would have been motivated to obtain the other. (Noelle Opposition 8, Paper No. 118, p. 21, Lederman Reply 8, Paper No. 129, p. 4).

b. Reasonable Expectation of Success

The parties disagree as to whether or not a reasonable expectation of success existed at the relevant date. Specifically, the parties disagree as to whether a person of ordinary skill in the art having either the anti-mouse or anti-human CD40CR antibodies would have had a reasonable expectation of success of obtaining the other.

A reasonable expectation of success is not a requirement of absolute predictability. Only a reasonable expectation that the beneficial result will be achieved is necessary to show obviousness. *Brown & Williamson Tobacco Corp. v. Philip Morris, Inc.*, 229 F.3d 1120, 1125, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000); *In re Longi*, 759 F.2d 887, 897, 225 USPQ 645, 651 (Fed. Cir. 1985). A critical step in analyzing these expectations is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the

prior art references and the then-accepted wisdom in the field. *In re Kotzab*, 217 F.3d 1365, 1369, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000).

Both parties have predominantly addressed their arguments and evidence to the issue of whether Noelle's claimed anti-mouse CD40CR antibodies would, in light of the prior art, have provided a reasonable expectation of success of obtaining Lederman's claimed anti-human CD40CR antibodies. Noelle justifies this focus by noting that its alleged prior art screening methodology works in either direction, i.e., mouse to human or human to mouse. (Transcript of Sept. 26, 2001 Oral Argument, Paper No. 134, p. 52, lines 1-10). As the parties have focused on the expectation of success for obtaining Lederman's claimed anti-human CD40CR antibodies, we adopt a similar focus.

Lederman argues that, as of the relevant date, there would not have been a reasonable expectation of success of obtaining a monoclonal antibody specific to human CD40CR antigen using a monoclonal antibody specific to mouse CD40CR antigen. (Paper No. 116, pages 16-17). Lederman further alleges that there were no processes available at that time for obtaining an anti-human CD40CR monoclonal antibody or its antigen with a reasonable expectation of success. (Paper No. 116, pages 17-19). Noelle disagrees.

According to Noelle, "the parties [sic] disclosures, coupled with the high level of skill in the art at the time, provided a reasonable expectation of success in making monoclonal antibodies to both the murine and human CD40CR antigens." (Paper No. 118, p. 3). Indeed, Noelle's expert, Dr. Edward Clark, has testified that Noelle's '480 application provided at least three different methods for making anti-CD40CR antibodies. (Declaration of Edward A. Clark,

NX 2012, p. 23, ¶ 30). Generally, the three methods mentioned by Dr. Clark are:

1) Immunization of a host with CD40CR expressing cells or cell line and selection of anti-CD40CR antibody by functional or competition binding with CD40Ig fusion protein;

2) Isolation of CD40CR by Affinity Purification using CD40Ig to precipitate at least human and mouse CD40CRs; and

3) Use MR1 monoclonal antibody or CD40Ig fusion to clone CD40CR DNA and use expression product to produce anti-CD40CR antibody.

(NX 2012, pages 23-33, ¶¶ 30-47). Noelle's opposition appears to focus upon an alleged reasonable expectation of success for the first method, immunization and screening, and the second method, using CD40Ig to co-precipitate its human counterpart ligand, human CD40CR.

Noelle's opposition argues that one skilled in the art had a reasonable expectation of success of obtaining Lederman's claimed anti-human CD40CR antibodies using immunization techniques, Dr. Clark's "first" method, or a precipitation technique involving a soluble CD40Ig protein, Dr. Clark's "second" method. Specifically, Noelle's opposition alleges that monoclonal antibodies to human CD40CR could be produced without undue experimentation since it was expected that CD40CR was expressed on activated human T-cells and:

> Also, it would be obvious to produce a population of hybridomas secreting monoclonal antibodies to activated human T-cell surface antigens and screen to identify those which express antibodies specific to CD40CR using known and available techniques. For example, a skilled person would have screened the hybridomas to identify monoclonal antibodies that block T-cell activation of B-cells. (NX 2012, ¶39). Such screening would not rise to the level of invention. The Federal Circuit has held particularly that routine screening of large populations of hybridomas does not constitute undue experimentation. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed Cir. 1988).
>
> The Noelle application teaches that monoclonal antibodies that specifically bind human CD40CR and T cells which express human CD40CR could be

> identified by use of the hCD40Ig fusion protein as a screen. On [sic] of ordinary skill would reasonably expect anti-human CD40CR antibodies to compete with soluble CD40Ig for binding to activated human T_h cells, and immunoprecipitate the same protein expressed on activated human T_h cells.

(Paper No. 118, pages 14-15).

During the oral argument of Sept. 26, 2001, Noelle appears to have moved away from its reliance on the teachings of its own specification. During the oral argument Noelle relied more upon a combination of allegedly conventional immunization and screening techniques. For instance, at oral argument, Noelle took the position that one skilled in the art had a reasonable expectation of success of obtaining the anti-human antibodies by a combination of: (1) activating T-cells; (2) immunizing a mouse with activated mouse or human T_h-cells and preparing hybridomas that produce the resulting antibodies; (3) conducting a "+/- screening" using activated and resting T-cells; and, (4) conducting functional screening. (See, Paper No. 133, Noelle Hearing Visual Aids, Tabs 1-6). Noelle also argued that one skilled in the art could immunoprecipitate the human CD40CR using CD40Ig. (See, Paper No. 133, Noelle Hearing Visual Aids, Tab 7).[6] Noelle's alleged expectation of success for the three methods said to be disclosed by the Noelle application as well as the methods specifically identified in Noelle's opposition and those identified at oral argument are discussed below.

i. Noelle's Reliance on the Parties' Specifications is Misplaced

At the outset, we note that Noelle's opposition relies extensively on the disclosures of the

[6]We commend both parties for the concise and informative visual aids that were provided at the oral argument of September 26, 2001.

Noelle and Lederman applications to provide one skilled in the art with a reasonable expectation of success of obtaining Lederman's claimed subject matter. For example, Noelle states:

> The parties' disclosures, coupled with the high level of skill in the art at the time, provided a reasonable expectation of success in making monoclonal antibodies to both the murine and human CD40CR antigens.

(Paper No. 118, p. 3). The parties' specifications, however, are not available as "prior art" for determining whether an interference-in-fact exists.

An interference-in-fact exists when:

> An *interference-in-fact* exists when at least one claim of a party that is designated ~~to correspond to a count and at least one claim of an opponent that is designated to~~ correspond to the count define the same patentable invention.

37 CFR § 1.601(j)(emphasis in original). The test for whether claims define the same or separate patentable inventions is as follows:

> Invention "A" is the *same patentable invention* as an invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A". Invention "A" is a *separate patentable invention* with respect to invention "B" when invention "A" is new (35 U.S.C. 102) and non-obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

37 CFR § 1.601(n)(emphasis in original). Thus, interference-in-fact questions require an analysis of whether or not a parties corresponding ***claims*** anticipate or render obvious the opposing parties corresponding ***claims***.

In determining whether an invention is a "separate" patentable invention, the parties specifications underlying the respective corresponding claims are not considered "prior art." The

specifications, however, could be relied upon to serve as a dictionary for the terms appearing in the claims or for admissions against interest regarding prior art.

Noelle's reliance on the parties specifications is misplaced. Specifically, Noelle has attempted to rely on the parties' disclosures as evidence that the claimed monoclonal antibodies could be produced without undue experimentation. For example, Noelle states that:

> [B]oth the ***Noelle and Lederman application*** **[sic]** ***similarly teach reproducible methods*** for producing monoclonal antibodies against an antigen (CD40CR) expressed by activated T cells and selecting appropriate (anti-CD40CR) monoclonal antibodies from the population of monoclonal antibodies obtained based on function or binding characteristics (inhibition of contact-dependent T/B cell activation, binding to an antigen expressed by activated T cells involved in B cell activation and/or competition with soluble human CD40-Ig for binding to activated T cells.) The ***Noelle application provides a reagent, soluble human CD40Ig***, that was a powerful tool for the identification of human CD40CR-expressing T cells for making monoclonal antibodies against human CD40CR or to affinity purify human CD40CR with a reasonable expectation of success.

(Paper No. 118, p. 18, lines 10-13, emphasis added). The parties corresponding claims are directed to: (i) monoclonal antibodies or fragments thereof; (ii) cell lines producing the antibodies and; (iii) pharmaceutical or diagnostic compositions containing the antibodies or fragments thereof. The corresponding claims are not directed to particular methods for producing monoclonal antibodies or to Noelle's CD40Ig fusion protein. As such, Noelle's opposition does not rely upon the parties' specifications to define the terms of the corresponding claims, but rather, Noelle relies upon the specifications as "prior art" references without showing how the specifications are admissions of, or references to, prior art. Accordingly, we discount those portions of Noelle's opposition that rely upon the parties' specification as evidence of an expectation of success.

antibodies that bind to activated helper T-cells and not to resting helper T-cells. (Paper No. 118, p. 20 and, Paper No. 133, Noelle Hearing Visual Aids, Tab 4). The functional screening technique involves testing a specific antibody to determine whether that antibody blocks T-cell activation of B-cells. (Paper No. 118, p. 14, Paper No. 133, Noelle Hearing Visual Aids, Tabs 5 and 6). The third screening technique, competitive binding assay, is based upon an alleged expectation that anti-human CD40CR antibodies would compete with soluble CD40Ig for binding to activated human T_h cells, and immunoprecipitate the same protein expressed on activated human T_h cells. (Paper No. 118, pages 15, 19).

At the outset, we note that Noelle has cited and relied upon the Federal Circuit's decision in *In re Wands* as evidence that screening was a known and available technique and that such screening would not rise to the level of invention. The situation in *Wands*, however, is distinguishable from the facts of the present case. Specifically, in *Wands* the starting materials, e.g., the HbsAg antigen, were available to the public whereas in the present case the CD40CR antigen was not available. 858 F.2d at 736, 8 USPQ2d at 1404.

At the relevant time, we find that the known existence of the mouse CD40CR antigen and the general conservation in function of immune cell molecules across species would have suggested the existence of the corresponding human CD40CR antigen. As such, one skilled in the art would have been motivated to identify and obtain anti-CD40CR antibodies via various conventional techniques, e.g., immunization and screening techniques. Yet, while the idea of using immunization and screening techniques to obtain anti-human CD40CR antibodies may have been obvious to try, the realization of that idea would not have been obvious. There were

ii. Prior Art Immunization Techniques Conventional But Lacked Reasonable Expectation of Success

According to Lederman, immunization techniques, such as those described in Noelle's application, would not have provided a reasonable expectation of obtaining a monoclonal antibody specific to human CD40CR. In particular, Lederman argues that there was no available reagent that would permit the specificity of the generated antibodies to be determined. Additionally, Lederman states that a person skilled in the art would not have been able to generate antibodies to the CD40CR antigen present on activated human T cell or cell membranes of activated human T cells as the kinetics of expression of the human CD40CR antigen were unknown at the relevant time and that CD40CR is not constitutively expressed on activated human T cells. (Paper No. 116, p. 18).

In contrast, Noelle argues that one skilled in the art would have had a reasonable expectation of success in producing a monoclonal antibody to the human CD40CR antigen. First, Noelle alleges that it would have been obvious to one of ordinary skill in the art to produce a set ("S1") of hybridomas that secrete monoclonal antibodies to activated human T-cell surface antigens. Once the population S1 had been generated, Noelle alleges that, using known and available techniques, one skilled in the art could then screen the population to identify those hybridomas that express antibodies specific to CD40CR. (Paper No. 118, p. 14).

Noelle's opposition cites three particular screening techniques, +/- screening, functional screening and competitive binding assay, that could be used to identify the desired hybridomas and their antibodies. (Paper No. 118, pages 14, 18 and 19). The +/- screening technique involves the testing population S1 of hybridomas to identify a subset ("S1a") of hybridomas that express

many potential pitfalls. Hindsight is not a justifiable basis on which to find that ultimate achievement of a sought after and difficult scientific goal was obvious. *See, Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991).

As argued by Lederman, one skilled in the art did not have a reasonable expectation th any particular activated human T cells expressed CD40CR. (Paper No. 116, p. 6, LX 1093, ¶ 53). Moreover, Lederman argues that one skilled in the art had no reasonable expectation of identifying which activated cells produced the required antigen or of isolating the antigen itsel (Paper No. 116, pages 6-7). Yet, Noelle's alleged immunization technique requires activated human T cells as a source of human CD40CR.

Noelle argues that one skilled in the art, using Noelle's CD40Ig, could have selected th appropriate T cells. (Paper No. 118, pages 15, 18 and 20). For example, Noelle states:

> Lederman also alleges that producing a monoclonal antibody against activated human T cells or T cell lines or membranes would be "complicated" by the fact that CD40CR is not constitutively expressed on activated human T cells. Noelle's response is that the ordinary (constitutive) expression not only was not necessary, the availability of activated cells expressing the antigen and resting cells that did not [express the antigen] provide a useful +/- screening tool. (NX 2087). ***The ordinarily skilled artisan would have known how to select T cells that express CD40CR on their cell surface using methods disclosed in the Noelle application***, e.g., based on their reactivity with human CD40Ig using flow cytrometry and a labeled hCd40Ig fusion protein. This procedure is disclosed at page 15, line 14 to page 16, line 2 of the ***Noelle application***, and would have been readily apparent to those skilled in the art. (NX 2012, ¶ 25).

(Paper No. 118, pages 19-20, emphasis added).

As discussed above, Noelle cannot rely upon the teachings of its application as "prior a evidence to demonstrate the obviousness of Lederman's corresponding claims. Moreover, as discussed below, one skilled in the art would not have possessed a reasonable expectation of

success of forming a CD40Ig fusion protein, which could then be used to obtain the claimed CD40CR antibodies. Thus, on this record, we conclude that Lederman has provided sufficient evidence to support a conclusion that, at the relevant time, one skilled in the art would not have had a reasonable expectation of success of identifying the activated T cells that produced the required CD40CR antigen or of isolating the antigen itself. Yet, we also conclude that Lederman has failed to provide sufficient evidence to convince us that this specific diminished expectation of success is, by and of itself, dispositive of the issue of whether one skilled in the art had a reasonable expectation of success of obtaining the parties claimed subject matter, i.e., the desired ~~antibodies or fragments thereof, cell lines and pharmaceutical compositions~~.

Even assuming that one skilled in the art had a reasonable expectation of success of identifying activated T-cell lines that expressed CD40CR, we conclude that the screening techniques cited by Noelle lacked a reasonable expectation of success. Noelle's +/- screening technique would lead to the identification of multiple antibodies and not just the claimed anti-human CD40CR antibody. The +/- screening technique merely creates a subset of antibodies "S1a" that bind to activated helper T-cells and not resting T-cells. Similarly, as there are many antibodies that inhibit B cell activation, Noelle's functional screening technique would lead to the identification of a subset ("S1b") of antibodies. Moreover, as discussed in detail below, one skilled in the art did not have a reasonable expectation of success of making a CD40Ig.

Noelle has failed to convince us that only the desired anti-CD40CR antibody is in both the S1a and S1b sets or that one skilled in the art could specifically identify and obtain the desired antibody out of the various screened subsets. As such, we are not convinced that one

skilled in the art, at the relevant date, would have a reasonable expectation of success that the anti-CD40CR antibodies could be obtained by the functional and +/- screening techniques, whether used alone or in combination.

We hold that the combination of Noelle's anti-mouse CD40CR antibodies, the motivatio to isolate the anti-human CD40CR antibodies and the conventional screening techniques of the prior art do not render Lederman's claimed anti-human CD40CR antibodies obvious, but at mos simply suggested a path of inquiry for an inventor to try.[7]

iii. Prior Art Construction of CD40-Ig Fusion Protein Lacked Reasonable Expectation of Success

Lederman argues that the use of a human CD40Ig fusion protein would not have enabled the production of human CD40CR as the synthesis of such a fusion protein, at the relevant date, would have been "extremely difficult." As evidence, Lederman cites our Memorandum (Paper No. 108), fact ¶ 33, which quotes from an affidavit made by Dr. Aruffo (LX 1009) during the prosecution of Noelle's parent U.S. Application No. 07/835,799. In the affidavit, Dr. Aruffo

[7] Additionally, we note Noelle has argued that the prior art to both Lederman and Noelle suggested the existence of the CD40CR antigen. (Paper No. 134, p. 38, lines 4-18). Noelle has also argued that one skilled in the art would have been motivated to obtain the antibodies to the CD40CR antigen. (Paper No. 134, p. 39, lines 6-14). Furthermore, Noelle has argued that it would have been obvious to obtain the antibodies via known and available immunization and screening techniques and that "such screening would not rise to the level of invention." (Paper No. 118, p. 14). As evident from the oral argument of September 26, 2001, if we accepted Noelle's contention that the prior art provided both: (1) the motivation to obtain the claimed anti CD40CR antibodies; and (2) conventional methods for which one skilled in the art had a reasonable expectation of success of obtaining the claimed anti-CD40CR antibodies, we could b led to a conclusion that the parties' claims were obvious over the prior art. As we find that, as o the relevant date, one skilled in the art did not possess a reasonable expectation of success, we need not explore this issue.

unequivocally stated that there was "not a reasonable expectation of success prior to the actual production of a recombinant immunoglobin fusion molecule." (LX 1009, p. 3).

Noelle, however, relies upon a CD40Ig fusion protein, such as that disclosed in Noelle's application, as a potential technique that could be used to immunoprecipitate CD40CR. (Paper No. 118, p. 15). Moreover, Noelle argues that the CD40Ig described in the Noelle application provides a "powerful tool for the identification of human CD40CR-expressing T cells." (Paper No. 118, p. 18).

Noelle contends that whether or not the formation of a CD40Ig fusion protein was unpredictable prior to Noelle's invention is not relevant to the facts of this case. Indeed, Noelle argues that whether the synthesis of this fusion protein and the properties thereof was unpredictable is a moot issue in light of the disclosure contained in Noelle's application. (Paper No. 118, pages 20-21).

As stated above, Noelle may not rely upon the teachings of its specification as evidence of the existence of a CD40Ig fusion protein. Moreover, we credit Dr. Aruffo's undisputed testimony with regards to the unpredictability and lack of a reasonable expectation of success of forming a CD40Ig fusion protein. From this, we conclude that one skilled in the art would not have possessed a reasonable expectation of success of forming a CD40Ig fusion protein, which could then be used to obtain the claimed CD40CR antibodies.

iv. Prior Art Expression Cloning Techniques Lacked Reasonable Expectation of Success

Additionally, while not argued by Noelle in its opposition or at oral argument, we take

this opportunity to reiterate our finding from the Memorandum regarding the third method mentioned by Dr. Clark, expression cloning, and the conclusions that flow from this finding. As set forth in the Memorandum, as of February 14, 1992, it would have been difficult for one of ordinary skill in the art to conduct the expression cloning methodology recited in the Noelle '48 application. (Paper 108, p. 16, fact 36). Moreover, as stated during the prosecution of U.S. Application 07/969,703:[8]

> "[A]pplicants submit that, at the time they began their efforts to clone a CD40-L [i.e., CD40CR], the skilled artisan could not have approached expression cloning with a reasonable expectation of success (this is still true today [October 1993])."

(October 1, 1993, Amendment and Response and Exhibits attached thereto, filed in U.S. Application 07/969,703, LX 1083). At the relevant time, we conclude that one of ordinary skill in the art would not have had a reasonable expectation of success of obtaining the desired anti-human CD40CR antibodies using a prior art expression cloning technique. (LX 1093 ¶¶ 32 and 33 and LX 1092, page 17, ¶ 45).

3. Lederman's "Human" Claims Would Not Render Obvious Noelle's "Mouse" Claims

Lederman argues that Noelle's "mouse" claims would have been unobvious over Lederman's "human" claims due to a lack of a reasonable expectation of success. Noelle, however, argues that one skilled in the art would have reasonably expected that a monoclonal antibody to mouse CD40CR could be generated by use of activated mouse T cells or membranes

[8]The 07/969,703 application is assigned to Immunex Corporation. The inventors of this application are said to be Dr. Richard Armitage, William C. Fanslow and Melanie K. Spriggs. Noelle did not request cross-examination of the inventors of this application.

as an immunogen, and screening for monoclonal antibodies that inhibit B cell activation and which bind to an antigen having a similar size to human CD40CR.

We concluded above that one skilled in the art lacked a reasonable expectation of success of obtaining Lederman's claimed "human" subject matter when provided with Noelle's "mouse" subject matter and using the screening techniques cited by Noelle. Likewise, we conclude that one skilled in the art would have lacked a reasonable expectation of success of obtaining Noelle's claimed "mouse" subject matter when provided with Lederman's claimed "human" subject matter and using these same screening methods. Additionally, we find that the alleged "similarity" in size does not help Noelle. Specifically, as noted by Lederman, the antigen bound by Lederman's anti-human CD40CR antibody is said to have a molecular weight of 30 kilodaltons whereas Noelle's anti-mouse CD40CR antibody binds an antigen that is said to have a molecular weight of 39 kilodaltons. (Paper No. 129, p. 8). Moreover, Noelle's expert, Dr. Clark, has testified that:

> [M]olecular weight determinations made by use of SDS-PAGE electrophoresis procedures are well known to be *subject to significant variability*, dependent upon factors including the extent of glycosylation of protein, the nature of polyacrylamide SDS gel, buffer conditions, among other factors.

(NX 2012, ¶ 26, emphasis added). Thus, one skilled in the art may have had doubts regarding the accuracy of the molecular weight determinations for the antigens. Furthermore, even if one skilled in the art were informed that Lederman's antigen had a molecular weight of 30 kilodaltons, it is unclear whether the person of ordinary skill in the art would have had a reasonable expectation of success of obtaining the mouse antigen, which was reported to have a molecular weight of 39 kilodaltons.

4. Dispute over Structural and Functional Obviousness

Lederman argues that a monoclonal antibody specific to human CD40CR antigen is structurally, chemically and functionally distinct from a monoclonal antibody specific to mouse CD40CR antigen. (Paper No. 116, p. 12). According to Lederman, because the structures and functions of the mouse and human antibodies are distinct and unobvious over each other, there is no interference-in-fact between the parties. Noelle disputes this contention. As we have determined that there was no reasonable expectation of success of obtaining either party's corresponding claimed subject matter starting from the others corresponding claims, this issue is moot.

V. Decision on Deferred Motions

Our Memorandum (Paper No. 108), deferred several preliminary motions. In particular, Lederman Preliminary Motions 1 and 2 were deferred and Noelle Preliminary Motions 1-4 were deferred.[9]

Noelle Preliminary Motions 1 and 3 request that the interfering subject matter be redefined. In light of our holding that none of Noelle's remaining corresponding patentable claims interferes with any of Lederman's corresponding claims, these motions are ***denied***.

Noelle Preliminary Motions 2 and 4 are contingent upon Noelle Preliminary Motions 1 and 3 and request priority benefit of an earlier filed Noelle application. As Noelle Preliminary Motions 1 and 3 are denied, Noelle Preliminary Motions 2 and 4 are also ***denied***.

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[9]Lederman Preliminary Motions 6 and 7 were also deferred, however, Lederman has withdrawn these motions from our consideration.

Lederman Preliminary Motions 1 and 2 generally request judgment against Noelle's "human" and "genus" claims on the grounds that they are unpatentable over prior art. Noelle, however, did not contest our finding that Noelle's "genus" and "human" claims lacked written descriptive support as of the February 14, 1992 filing date and did not contest the unpatentability of these claims under 35 U.S.C. §102(b). We note, however, that Lederman Preliminary Motion 1 does allege that certain Noelle "mouse" claims are unpatentable over prior art. In light of our decision that there is no "interference-in-fact" and as Noelle's claims are present in a pending U.S. application, a determination as to the patentability of Noelle's mouse claims is best resolved outside the course of this interference. Moreover, it is our understanding that Lederman has agreed to this procedure. Thus, Lederman Preliminary Motions 1 and 2 are dismissed as ***moot***.

VI. Conclusion

Lederman has demonstrated that, as of the relevant date, one of ordinary skill in the art would not have had a reasonable expectation of success of obtaining an anti-mouse CD40CR antibody or an anti-human CD40CR antibody. Accordingly, we hold that Lederman has established that its claimed "human" embodiment is patentably distinct from Noelle's claimed "mouse" embodiment and *vice-versa*. Thus, we ***grant*** Lederman Preliminary Motion 8.

VII. Order

It is:

ORDERED that Lederman Preliminary Motion 8 is ***granted***.

FURTHER ORDERED that no interference-in-fact exists between claims 1-7 and 10-13 of Lederman, U.S. Patent No. 5,474,771 and claims 42, 43, 46-48, 50, 54, and 57 of Noelle, U.S. Application No. 08/742,480.

FURTHER ORDERED that Noelle is not entitled to a patent containing claims 51, 52, 53, 56, 59 and 60 of Noelle, U.S. Application No. 08/742,480.

FURTHER ORDERED that a copy of this final decision shall be placed and given a paper number in the file of Lederman, U.S. Patent No. 5,474,771 and Noelle, U.S. Application No. 08/742,480.

RICHARD TORCZON
Administrative Patent Judge

SALLY GARDNER-LANE
Administrative Patent Judge

MICHAEL P. TIERNEY
Administrative Patent Judge

BOARD OF PATENT
APPEALS
AND
INTERFERENCES

cc: (via Federal Express)

Counsel for Noelle:

Anthony Figg
ROTHWELL, FIGG, ERNST & MANBECK, PC
555 Thirteenth Street, NW
Washington DC 20004
Tel: (202) 783-6040
Fax: (202) 783-6031

Counsel for Lederman:

James F. Haley, Jr., Esq.
Margaret A. Pierri
Jane T. Gunnison
Stanley D. Liang
FISH & NEAVE
1251 Avenue of the Americas, 50th Floor
New York, New York 10020
Tel: (212) 596-9000
Fax: (212) 596-9090

CERTIFICATE OF COMPLIANCE

Counsel for Appellant Randolph J. Noelle certifies that this brief complies with the type-volume limitation of Fed. R. App. P. 32(a)(7)(B)(i). The number of words in this brief, excluding the items that do not count towards the limitation under Fed. R. App. P. 32(a)(7)(B)(iii) and Fed. Cir. R. 32(b), is 10,983.

E. Anthony Figg /6EK

E. Anthony Figg
COUNSEL FOR APPELLANT
RANDOLPH J. NOELLE

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

02-1187
(Interference No. 104,415)

RANDOLPH J. NOELLE,

Appellant,

v.

SETH LEDERMAN, LEONARD CHESS, and MICHAEL J. YELLIN,

Appellees.

Appeal from the United States Patent and Trademark Office,
Board of Patent Appeals and Interferences

BRIEF OF APPELLEES SETH LEDERMAN, LEONARD CHESS, and MICHAEL J. YELLIN

James F. Haley, Jr.
Margaret A. Pierri
Jane T. Gunnison
FISH & NEAVE
1251 Avenue of the Americas
New York, New York 10020
(212) 596-9000

John P. White
COOPER & DUNHAM LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

May 23, 2003

CERTIFICATE OF INTEREST

Counsel for the Appellees SETH LEDERMAN, LEONARD CHESS and MICHAEL J. YELLIN certifies the following:

1. The full name of every party or amicus represented by me is:

Seth Lederman, Leonard Chess and Michael J. Yellin.

2. The name of the real parties in interest (if the party named in the caption is not the real party in interest) represented by me are:

The Trustees of Columbia University in the City of New York;

Biogen, Inc.;

(The United States of America may have rights to Lederman et al.'s United States Patent 5,474,771 pursuant to Grant Nos. PO1-AI-26886; RO1-AI-14969 and Immunology Training Grant AI-07132 awarded by the National Institutes of Health).

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

None.

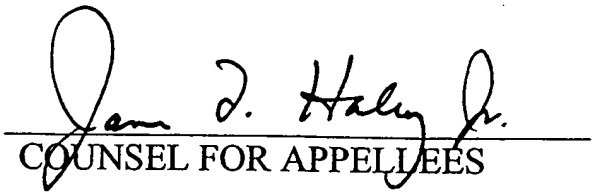
4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or

agency or are expected to appear in this Court are:

Fish & Neave: James F. Haley, Jr., Margaret A. Pierri and Jane T. Gunnison.

Cooper & Dunham LLP: John P. White.

May 23, 2003



COUNSEL FOR APPELLEES

FISH & NEAVE
James F. Haley, Jr.
Margaret A. Pierri
Jane T. Gunnison
1251 Avenue of the Americas
New York, New York 10020
Tel.: (212) 596-9000
Fax.: (212) 596-9090

COOPER & DUNHAM LLP
John P. White
1185 Avenue of the Americas
New York, New York 10036
Tel.: (212) 278-0400
Fax.: (212) 391-0525

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STATEMENT OF RELATED CASES

No other appeal from this patent interference was previously before this or any other appellate court.

Lederman is aware that Noelle has appealed to this Court from a decision of the Board of Patent Appeals and Interferences ("the Board") in a patent interference between Noelle and Armitage et al. *See* Appeal No. 03-1361. JA4188-4211. Lederman understands that the "mouse" claims of the Noelle application at issue here were involved in that interference and that the Board held those claims to be unpatentable to Noelle as not enabled. The status of Noelle's appeal or related appeals is unknown.

I. STATEMENT OF THE ISSUES

The Board's decision should be affirmed. In reaching its decision, the Board correctly applied the relevant legal precedent. Its decision is also supported by substantial evidence. The Board properly and correctly held that Noelle's human and genus claims were unpatentable to him and that no interference-in-fact existed between Noelle's remaining mouse claims and Lederman's human claims.

The issues before the Court distill to two[1]:

Whether the Board was correct in holding that Noelle's claims to monoclonal antibodies ("mAbs") specific to the human CD40 counter receptor ("CD40CR") antigen ("Noelle's human claims") and to a genus that includes, *inter alia*, those mAbs ("Noelle's genus claims") were not entitled to the benefit of the February 14, 1992 filing date of Noelle's grandparent application because that application did not describe any human CD40CR antigen or any mAb to that antigen except by function -- one binds to the other?

Whether the Board was correct to refer to Noelle's specification for definitional purposes only and not to consider his disclosure as part of the prior art when the Board held that there was no interference-in-fact between Noelle's mouse claims and Lederman's human claims?

II. STATEMENT OF THE CASE

The single count in interference recites three alternatives: mAbs specific to a human CD40CR antigen; mAbs specific to a mouse CD40CR

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[1] Noelle's four issues are really two. Noelle has admitted that, absent benefit from the filing date of his '799 application, his genus and human claims are unpatentable over the prior art. N.Br. 4. And, contrary to Noelle's assertions, the Board did not rely on the two-way test for no interference-in-fact. It held that whether mouse or human claims were assumed to be prior art, the other was patentable.

antigen; and a genus of mAbs specific to CD40CR antigens from any species. JA00032-76 at JA00035.

Noelle's application in interference ("the '480 application") has claims directed to each alternative of the count. JA00035. Lederman's United States patent 5,474,771 ("the '771 patent") has claims directed solely to the human alternative. JA00035. None of the parties' claims that correspond to the count *is* directed to methods for producing monoclonal antibodies to CD40CR antigens, or to Noelle's CD40-Ig fusion protein. Each recites only a monoclonal antibody. JA00001-31 at JA00019.

This interference was decided on preliminary motions. Neither party submitted a priority case.

In the first stage of the interference -- unpatentability of Noelle's claims -- the Board held that Noelle's genus and human claims were not entitled to benefit of the February 14, 1992 filing date of his '799 application under 35 U.S.C. § 120. As a result, the Board ruled that those claims were unpatentable as anticipated by the prior art under 35 U.S.C. § 102(b). JA00065; JA03822-JA03835.

In the second stage of the interference -- no interference-in-fact between Lederman's human claims and Noelle's mouse claims -- the Board considered patentability by two separate one-way tests -- mouse to human

and human to mouse. It held on the one hand that "one skilled in the art, provided with Noelle's 'mouse' claims and the prior art, would not have a reasonable expectation of success of obtaining the anti-human antibodies." JA00004. On the other hand, the Board held that "one skilled in the art would have lacked a reasonable expectation of success of obtaining Noelle's claimed 'mouse' subject matter when provided with Lederman's claimed 'human' subject matter and using [the screening techniques cited by Noelle]." JA00027, ll. 6-8. Thus, the Board ruled that no matter whether the mouse claims or the human claims were assumed to be prior art, the other was patentable.

At no time did Noelle argue, as he does here, that the Board, having found some of Noelle's claims unpatentable to him and having found the rest of his claims not to interfere with Lederman's claims, should have still determined priority. N.Br. 37-8.

III. STATEMENT OF THE FACTS

A. CD40CR, The Immune Response, And Skill In The Art

In at least mice and humans, it is *now* understood that B cell activation results from the interaction of CD40CR antigen, a protein on the surface of activated helper T cells, with CD40, a protein on the surface of B cells. JA00529-554 at JA00535. B cell activation initiates the immune

response. JA00288, col. 1, ll. 22-9; JA3836-67 at JA3827. MAbs specific to CD40CR antigen are also *now* known to be capable of inhibiting B cell activation and, thus, the immune response. JA00041; JA00535. The state of the art was much different at the February 14, 1992 filing date of Noelle's first patent application.[2]

As of February 14, 1992, a person skilled in the art knew that T cells existed in all vertebrates. JA00535; JA4234-60 at JA4245-6, ¶ 26. One skilled in the art at that time also recognized the induction of B cells to be a complex process, in which the precise mechanisms of T cell stimulation of B cells were unclear and a variety of receptor ligand interactions appeared to be involved. JA00010-11. One skilled in the art of B cell responses, as of February 14, 1992, however, would not have extrapolated information about anti-mouse CD40CR antibodies to anti-human CD40CR antibodies because "differences between the regulation of human and murine B cells make it additionally difficult to extrapolate the results obtained from one system to another." JA00012 (internal citation omitted).

As of February 14, 1992, the isolation and purification of CD40CR antigens was not predictable. JA00048. And, at that date, the

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2 Noelle's grandparent application 07/835,799 was filed February 14, 1992.

skilled worker would have expected CD40CR antigens from different species, to the extent they even existed, to "vary considerably in size, structure, chemical composition and/or function." JA00535.

As of February 14, 1992, the person skilled in the art was familiar with methods for generating monoclonal antibodies that specifically bind antigens. JA00048. At that date, "once in possession of an antigen, such as a particular CD40CR, a person of ordinary one of skill in the art could readily make a monoclonal antibody that specifically binds to that antigen." JA00042.

B. The Written Description Of Noelle's Grandparent '799 Application[3]

1. Noelle Described An Anti-Mouse CD40CR MAb And A Mouse CD40CR Antigen

Noelle's '480 application describes one mAb ("MR1") that binds specifically to a mouse CD40CR antigen. Indeed, Noelle deposited cells that produced that mAb. JA00043, ¶ 17.

Noelle described the mouse CD40CR antigen as a 39 kilodalton ("kD") protein on the surface of activated mouse T cells. JA00045;

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[3] The specifications of Noelle's '799 and '480 applications are identical. The '480 application is a continuation (through the '975 application) of the '799 application. JA00038.

JA04248, ¶ 32. Noelle characterized the 39kD protein (the mouse antigen) by its specific binding to the deposited MR1 antibody. JA01759-JA01783 at JA01762, ¶ 8. Thus, one side of the binding pair was part of Noelle's application.

With Noelle's MR1 antibody in hand, a person skilled in the art could isolate the 39kD mouse protein. JA01762, ¶ 8; JA01208, ll. 9-20. With Noelle's 39kD mouse CD40CR antigen in hand (*i.e.*, as purified using the MR1 antibody), the skilled worker could make and isolate another mAb that specifically binds to it. JA00041, ¶ 14.

2. Noelle Did Not Describe A Genus Of Anti-CD40CR MAbs Or A Genus Of CD40CR Antigens

Noelle's '799 application provided no structural or physical characteristics of a mAb specific to any non-mouse CD40CR antigen. JA00063, ll. 5-8; JA00539, ¶ 21; JA00553, ¶ 51. Nor did Noelle deposit any cells that produced any mAb to a non-mouse CD40CR antigen. And, Noelle's '799 application did not provide any non-mouse CD40CR antigen or describe such antigen in terms of its structural or physical characteristics. JA00540, ¶ 22; JA4245, ¶ 24. The application referred only to a single mouse CD40CR antigen (39kD) and its antibody (MR1).

Noelle concedes that the '799 application does not identify a genus of anti-CD40CR antibodies by structure. At best, the application refers to function, *i.e.*, the unidentified antibodies bind to the unidentified CD40CRs and vice versa. JA00063, n.11; JA4065, l. 18 to JA4066, l. 7; JA4066, ll. 14-22. Yet, Noelle did not identify any correlation between the binding function of anti-CD40CR antibodies and their unidentified structure. Thus, Noelle's "disclosure" is at best a statement of the common general knowledge -- an antibody binds to its antigen; an antigen binds to its antibody. Noelle's "disclosure" is analogous to a statement that a DNA encodes its protein and the protein is encoded by its DNA. It certainly is not a disclosure of any specific or representative member of the claimed genus.

Finally, Noelle's '799 application does not define any structural or physical features that are common to Noelle's specific mouse CD40CR antigen (the 39kD protein) or mAb (MR1) and any other CD40CR antigen or antibody. JA00049; JA00536; JA00558; JA00540.

In light of the lack of disclosure in Noelle's '799 application of any non-mouse antigen or antibody, the Board found:

> The Noelle '480 application requires that one skilled in the art make certain assumptions as to non-mouse CD40CRs and their antibodies. . .

JA 00049, ll. 11-12.

> Noelle presents claims to a genus and to a particular species, human, while describing only one species (mouse). Indeed, the specification in . . . Noelle fail[s] to describe any structural features commonly possessed by the member[s] of the genus that distinguish them from others such that one skilled in the art may recognize the identity of members of the genus.

JA00062, ll. 10-13.

The Board also correctly found:

> As of February 14, 1992, the isolation and purification of CD40 counter receptors ("CD40CR") was *not* a predictable art. As of this date, the skilled artisan could not have predicted with any reasonable degree of certainty from Noelle's disclosure whether particular CD40CRs and the antibodies specific to the CD40CRs could be generated and isolated other than Noelle's disclosed mouse CD40CR and the antibodies specific to the mouse CD40CR. Indeed, it would have been difficult for the skilled artisan to generate and isolate the CD40CRs and antibodies specific to the CD40CRs beyond those disclosed by Noelle's application.

JA00048, ¶ 32 (internal citations omitted; emphasis in original).

3. Noelle Does Not Describe An Anti-Human CD40CR MAb Or A Human CD40CR Antigen

Noelle's '799 application does not provide any structural or physical characteristics of a mAb specific to human CD40CR antigen. JA00539, ¶ 21; JA00553, ¶ 51. And Noelle did not deposit any cells that made such antibody. Nor does Noelle's '799 application provide any structural or physical characteristics of a human CD40CR antigen, to the extent it even existed. JA00539-40, ¶¶ 21-2; JA00063, ll. 5-8. Rather, in the

context of the human antigen and antibody, Noelle states only the basic dogma of antibodies and antigens -- one binds to the other. JA00040, ¶ 9.

Neither Noelle's mouse MR1 antibody nor 39kD mouse CD40CR antigen provided any information about the human antibody or antigen. Noelle's MR1 mouse antibody does not bind to and cannot be used to isolate a human CD40CR antigen. JA0535-6, ¶ 11; JA4246, ¶ 28. And, Noelle's mouse CD40CR antigen (the 39kD protein) cannot be used to make or isolate a mAb to a human CD40CR antigen. JA00535-6, ¶ 11; JA00547, ¶ 38. The mouse antigen does not bind to the human antibody. JA00539, ¶ 21.

The Noelle '799 application also does not describe any structural or physical feature that is common to mouse and human CD40CR antigens or their antibodies. JA00062; JA00066, ll. 14-22. As the Board noted, even the sizes of those antigens were different:

> [T]he alleged "similarity" in size does not help Noelle. Specifically, . . . the antigen bound by Lederman's anti-human CD40CR antibody is said to have a molecular weight of 30 kilodaltons whereas Noelle's anti-mouse CD40CR antibody binds an antigen that is said to have a molecular weight of 39 kilodaltons.

JA00027, ll. 8-12 (internal citation omitted). And, the fact that the mouse antigen and antibody do not bind to their human counterparts establishes

without a doubt that the structures of the two antigens and the two antibodies are different. JA00539; JA00556-7; JA00553.

For all of these reasons, the Board correctly held that Noelle's '799 application lacked written description for his claimed anti-human CD40CR mAb. As the Board found: Noelle failed to describe any of the antibody's structural or physical features, and did not describe any of the structural or physical features of a human CD40CR antigen from which the mAb might have been made. JA00062, ll. 14-16. Absent a description of either the human antibody or the human antigen, a person skilled in the art would not believe that Noelle was in possession of the claimed anti-human CD40CR mAb. JA00048, ¶ 32.

C. Noelle's Proposed Methods Of Obtaining An Anti-Human CD40CR MAb Or Human CD40CR Antigen Would Not Work And Provide No Written Description For The Claimed Antibodies

Noelle's expert, Dr. Clark, testified that the '799 application provided several methods for making anti-human CD40CR antibodies. JA01214-5, § 6.1.7; JA00015-16; JA03515-6, ¶ 30.

As summarized by the Board, three of the methods were:

> 1) Immunization of a host with CD40CR expressing cells or cell line and selection of anti-CD40CR antibody **by functional or competition binding with CD40-Ig fusion protein**;

2) Isolation of CD40CR by affinity purification **using CD40-Ig to precipitate** at least human and mouse CD40CRs; and

3) **Use of** MR1 monoclonal antibody or **CD40-Ig fusion to clone** CD40CR DNA and use of expression product to produce anti-CD40CR antibody.

JA00016, ll. 2-8 (emphasis added). All relied on a "CD40-Ig fusion protein" referred to in the '799 application.

None of these methods would work. Noelle's CD40-Ig fusion protein could not have been used to isolate either a human CD40CR antigen or a mAb that binds it. JA01740-01758 at JA01761-7; JA00050, ¶ 35; JA00560-1; JA00573-4. More importantly, even if the CD40-Ig fusion could be used, the '799 application would still not satisfy the written description requirement for claims to mAbs to CD40CR. Methods of producing do not provide written description for a compound. *See infra,* p. 29.

There are several reasons why Noelle's attempt to rely on CD40-Ig is a strawman. First and foremost, as of February 14, 1992, production of Noelle's CD40-Ig reagent would have been extremely difficult. JA00048-49, ¶ 33; JA01763, ¶ 10; JA01746-7, ¶ 16; JA04252, ¶ 40.

Further, "[i]mmunization with activated human T cells or activated or non-activated [human T] cell lines, such as Jurkat and HSB2,

would raise antibodies to a number of known and unknown T cell proteins such as CD4, OX40 receptor, CD25, MHC class II and ICAM-1.[22] JA00012, ¶ 44 (internal citation omitted). Selecting an anti-human CD40CR antibody from the resulting population of diverse antibodies would be difficult without a human CD40CR-specific reagent. No such reagent existed in the prior art. And, Noelle disclosed none. Certainly, CD40-Ig does not fit the bill.

While Noelle argues that his '480 application suggests that the CD40-Ig fusion binds to human T cell lines, the experiment to which he points does not include the necessary controls. Thus, there is no evidence that the reported binding is specific to CD40CR antigen or even due to the CD40 portion (which is the portion that would bind, *inter alia*, to the CD40CR antigen were it to exist on activated human T cells). Indeed, the binding may have been through the Ig portion (which may bind to other compounds on the surfaces of a human T cell). JA00046, ¶ 26; JA01761-JA01765.

As the Board explained:

> One skilled in the art reviewing the Noelle '480 application would have doubts regarding the validity of Section 7 [which discusses the binding of a CD40-Ig fusion protein to human T-cell lines]. Specifically, a control should have been included in Section 7 to confirm that the reported binding is due to the CD40 moiety, rather than the Ig moiety, of the CD40-Ig fusion

> protein. . . . Absent the proper control, one skilled in the art could not have known whether the CD40-Ig fusion protein was binding to a cell surface protein on Jurkat and HSB2 cells via the CD40 portion of the CD40-Ig molecule.

JA00050, ¶ 35 (internal citations omitted).

Even Noelle's expert, Dr. Clark, agreed that "such a control should have been conducted." JA03501, ll. 12-3. Noelle likewise has admitted that he had no evidence that the CD40-Ig fusion protein actually bound to a human CD40CR:

> [D]id we ever take and isolate CD40CR -- or does our application? Let's put it that way. Does our application ever do that, or did we ever put in proof that what this human CD40-Ig was binding to was the material that we thought it was? No.

JA4106, ll. 2-8.

And, when Noelle finally identified a human CD40CR antigen, almost a year after filing the '799 application, he first mutated the CD40-Ig fusion protein disclosed in the application. The mutation modified the Ig portion of the fusion to reduce its ability to bind particular non-CD40CR antigens on cells. JA01504-16 at 1510, right col., ll. 17-20; JA01752; JA01703-4; pp. 112-5; JA01764. ¶ 14.

In addition to these CD40-Ig specific methods, Noelle has also proposed using +/- screening (i.e., screening for mAbs that bind activated, but not resting, T cells) to identify antibodies that bind CD40CR antigen.

JA00262. Again, at best, this is a description of a method for obtaining an antibody, not a description of the antibody itself. More importantly, +/- screening provides no reasonable expectation of success for obtaining an anti-human CD40CR mAb. The method only identifies antibodies that bind to any of the large number of antigens that are present on activated, but not on non-activated, T cells. JA00023; JA3885. The evidence shows that the CD40CR antigen is far from the only antigen potentially produced by activated, but not resting, T cells. JA00023.

Finally, Noelle proposed using expression cloning to isolate a human CD40CR antigen. Expression cloning is a putative method for obtaining the antigen. It is not a description of the CD40CR antigen itself or its antibody. Furthermore, as of February 14, 1992, it would have been beyond the skill of the art to carry out expression cloning successfully. JA00050, ¶ 36.

D. Lederman's '771 Patent Describes Both A Human CD40CR Antigen And Its Antibody

In the context of a disclosure of the human CD40CR antigen and its antibody, the contrast between Noelle's application and Lederman's patent is striking.

Lederman's '771 patent describes and enables a monoclonal antibody ("5c8") that binds specifically to a human CD40CR antigen. Lederman described the human antigen as a 30kD protein on the surface of activated human T cells and on D1.1 cells, a mutated form of human T cells that constitutively express human CD40CR antigen on their surface. JA00298, Ex. 4; JA01043-54.

Evidencing his possession of both the human antibody and the human antigen, Lederman deposited cells that make the 5c8 antibody and deposited the D1.1 cells that continuously make the antigen. JA00828. With Lederman's 5c8 antibody in hand, a person skilled in the art could readily purify the 30kD human protein. JA00298, Ex. 4; JA00291, col. 8, ll. 1-3. With Lederman's 30kD human CD40CR in hand, a person skilled in the art could readily make and isolate other mAbs to a human CD40CR antigen. JA00551, ¶ 46; JA04243, ¶ 18.

E. There Is No Interference-In-Fact Between Noelle's Mouse Claims And Lederman's Human Claims

1. Novelty

A monoclonal antibody specific to a mouse CD40CR antigen is not identical to a monoclonal antibody specific to a human CD40CR antigen. JA00013. This is admitted. Thus, Noelle's mouse claims do not anticipate Lederman's human claims and vice versa.

2. Non-Obviousness

At the relevant date, the skilled worker "having [in hand either] anti-human CD40CR antibodies or anti-mouse CD40CR antibodies would have been motivated to [try to] obtain the other." JA00014. There was, however, no method available that would have reached that goal with a reasonable expectation of success. JA00020-6.

As we have explained above, there was no method for obtaining an anti-human CD40CR mAb with a reasonable expectation of success, even if Noelle's anti-mouse CD40CR mAb were part of the prior art. JA00020-6. And, this is true even if Noelle's CD40-Ig fusion protein had also been available in the prior art (which it was not). JA01761-7; JA01746-53. *See* discussion *supra*, p. 13.

For the same reasons, there was no method of obtaining an anti-mouse CD40CR mAb with a reasonable expectation of success, even if the prior art included Lederman's anti-human CD40CR mAb. JA00026-7.

Thus, irrespective of the direction analyzed -- mouse to human or human to mouse -- the two antibodies are not obvious over one another.

IV. SUMMARY OF THE ARGUMENT

The Board's findings of fact resulted from a thoughtful and careful consideration of the evidence that each party presented. Properly

weighing the totality of that evidence, the Board held that Noelle's genus and human claims were unpatentable to him and ruled that there was no interference-in-fact between Noelle's only remaining claims -- the mouse claims -- and Lederman's human claims, whichever was assumed to be part of the prior art.

This appeal is not a vehicle for *de novo* review of the evidentiary record. Nor is this Court a venue for issues never raised below. The decision of the Board should be affirmed. It is supported by substantial evidence. It is proper as a matter of law.

In this appeal, Noelle continues to argue that reference to the dogma of antibody/antigen function -- they bind to each other -- is enough to provide a written description of a specific antigen -- human CD40CR antigen -- and a specific antibody -- a mAb to human CD40CR. This makes a mockery of written description and elevates words over substance.

There can be no dispute that Noelle's application does not describe any physical or structural characteristic of a human CD40CR antigen or its antibody. Nor does Noelle describe any physical or structural feature that the supposed human antigen shares with Noelle's 39kD mouse antigen or that the supposed human antibody shares with Noelle's MR1 mouse antibody. Indeed, the antigens are of different sizes and do not cross

react with antibodies of the other species. And, the antibodies do not bind to the same antigen. Thus, structurally both antigens and antibodies are very different. And, Noelle has not said what those differences are.

Implicitly conceding his lack of description, Noelle tries to create the impression that he discloses a number of methods that would produce the human CD40CR antigen or antibody. Not true. First, methods of obtaining a compound are no substitute for a written description of the compound itself. Furthermore, the evidence makes plain that none of Noelle's speculative methods would have produced the hoped-for antigen or antibody with a reasonable expectation of success.

Furthermore, there was no evidence that the key reagent required in many of Noelle's methods, CD40-Ig, could even be made or, if made, used to isolate a human CD40CR antibody or antigen. And, when Noelle finally did report isolation of the human CD40CR antigen -- almost one year after the filing date of his first application, he did not use that CD40-Ig. He mutated it to avoid binding to cells through the Ig portion of the fusion. That portion does not bind to a CD40CR antigen.

In stark contrast, Lederman has fully described the physical and structural characteristics of his anti-human CD40CR antibody (5c8) and his

human CD40CR antigen (30kD) and actually deposited cell lines that produce both of them.

Challenging the Board's no interference-in-fact ruling, Noelle argues that the Board improperly relied on the two-way test. Not so. The Board specifically ruled that whether the claimed mouse CD40CR antibody or the claimed human CD40CR antibody were assumed to be prior art, the other was patentable.

Noelle's final contention, that the Board should have considered Noelle's CD40-Ig fusion protein when assessing the separate patentability of the human CD40CR antibody misapprehends the law. It is the claims, not the respective applications in interference, that must be assessed in determining interference-in-fact. And, even if the Board had included CD40-Ig as part of the prior art (which it was not), its no interference-in-fact decision would not have changed one iota. As the evidence demonstrates, the skilled worker would have had no reasonable expectation of success of isolating a human CD40CR antigen or antibody using the CD40-Ig fusion protein. Indeed, even Noelle did not do that. He modified the fusion before he used it to identify a human CD40CR antigen.

V. ARGUMENT

A. The Standard Of Review

Written description is a question of fact. *Enzo Biochem, Inc.* v. *Gen-Probe Inc.*, 323 F.3d 956, 962-3, 63 USPQ2d 1609, 1611, 63 USPQ2d 1618 (Fed. Cir. 2002).

Obviousness is a question of law, based on underlying findings of fact. "A determination of obviousness under 35 U.S.C. § 103 is a legal conclusion involving factual inquiries." *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1570, 41 USPQ2d 1961, 1964 (Fed. Cir. 1997).

This Court reviews the Board's determinations of fact under the substantial evidence standard. *In re Gartside*, 203 F.3d 1305, 1316, 53 USPQ2d 1769, 1776 (Fed. Cir. 2000). "The 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Gartside*, 203 F.3d at 1312, 53 USPQ2d at 1773.

This Court reviews matters of law *de novo*. *Loral Fairchild Corp.* v. *Sony Corp.*, 181 F.3d 1313, 1320, 50 USPQ2d 1865, 1869 (Fed. Cir. 1999).

B. The Board Correctly Ruled That Noelle Had No Written Description For His Genus And Human Claims

Noelle asserts that the Board departed from established legal precedent or misapplied the correct precedent to the monoclonal antibody

technology of the claims in interference. N.Br. 4. Noelle also contends that the Board confused possession of the invention with possession of physical materials resulting from its actual reduction to practice. N.Br. 8. This, according to Noelle, conflated the separate requirements of written description and enablement. N.Br. 26-7. Noelle is mistaken.

As we will demonstrate, the Board properly applied the correct legal precedent when it ruled that a general statement of function -- an antibody binds to an antigen -- is not written description of a specific antigen or specific antibody. The Board also correctly ruled that, without a disclosure of common physical or structural features, a mouse mAb could not provide the necessary written description of a human mAb or of genus of mAbs of various species.

As we will also demonstrate, substantial evidence supports the Board's holdings of no written description. The Noelle application provides no structural or physical features of any anti-CD40CR antibody except mouse MR1. The Noelle application describes no common physical or structural features that characterize the genus of CD40CR antibodies or CD40CR antigens. Even the size of the human and mouse CD40CR antigens are very different. Further, the mouse antibody does not bind the human antigen nor does the human antibody bind the mouse antigen.

JA00535-6, ¶ 11; JA00539, ¶ 21. Thus, the structure of both antigens and antibodies are also very different.

1. The Board Followed The Correct Legal Precedent And Properly Applied It To Noelle's Claims

For a claim to be entitled to benefit of a parent application, the application must provide written descriptive support for it. *In re Ruschig*, 379 F.2d 990, 154 USPQ 118 (C.C.P.A. 1967). Likewise, for a claim to be patentable under 35 U.S.C. § 112, first paragraph, the specification must provide a written description of every one of its elements. *Regents of Univer. of Cal.* v. *Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

The test for written description is whether the skilled artisan would discern from the application that the inventors had possession of the invention. *Moba, B.V.* v. *Diamond Automation*, 325 F.3d 1306, 1320-21, 66 USPQ2d 1429, 1439 (Fed. Cir. 2003). *See* N.Br. 8.

For chemical compounds, like the mAbs claimed here, written description requires a definition by structure or physical characteristics or requires some other means of distinguishing the claimed compound from unrelated substances. *Oka* v. *Youssefyeh*, 849 F.2d 581, 583, 7 USPQ2d

1169, 1171 (Fed. Cir. 1988); *Amgen, Inc.* v. *Chugai Pharm. Co. Ltd.*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).

Applying that precedent to one type of chemical compound, DNA, this Court held in *Lilly* that "[a]n adequate written description of a DNA . . . 'requires a precise definition, such as by structure, formula, chemical name, or physical properties.'" *Lilly*, 119 F.3d at 1566, 43 USPQ2d at 1404. *See also Fiers* v. *Revel*, 984 F.2d 1164, 1169, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993).

The *Lilly* and *Fiers* decisions are not limited to DNA, as Noelle contends. N.Br. 35. They apply generally. *See, e.g., Moba, B.V.*, 325 F.3d at 1320, 66 USPQ2d at 1438-9 (*Lilly* and *Enzo* are appropriate precedent for any written description case, not just for claims directed to genetic materials); *Univer. of Rochester* v. *G.D. Searle & Co.*, 249 F. Supp. 2d 216 (W.D.N.Y. 2003) (the Court was not persuaded that the holdings of *Enzo*, *Lilly* and *Fiers* were limited to claims directed to DNA. That assertion was not supported by the language of the cases themselves).

Noelle asserts that the Board improperly extended the "fact-specific holdings" of *Lilly* and *Fiers* to the "substantially different facts and technology of this case." N.Br. 35. Noelle is mistaken. It is the claims that determine the metes and bounds of the required written description. Here,

these claims are to a mAb -- a type of chemical compound. The claimed DNA of *Lilly* and *Fiers* was another type of chemical compound. Thus, the logic of *Lilly*, *Fiers* and the other prior written description-chemical compound cases (*e.g.*, *Oka* and *The University of Rochester*) applies four square here.

The facts here are strikingly similar to those in *Lilly*. Just like in *Lilly*, Noelle has not defined his claimed compound by any structural or physical property. Noelle, just like the Regents, has also pointed to one mammalian species as supposedly providing the necessary written description of another. Yet, Noelle, like the Regents, never possessed the claimed human species. Instead, like the Regents, Noelle tries to rely on the general function of the claimed compound. Compare the Regents' function (it codes for human insulin) to Noelle's function (it binds human CD40CR antigen).[4] In fact, Noelle's disclosure is far less than the Regents' disclosure. The Regents at least had possession of human insulin (it was in the prior art). Noelle did not have possession of any human CD40CR. At best, Noelle speculated that the human antigen existed. However, Noelle

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[4] *University of Rochester* (249 F. Supp. 2d 216) is also apposite. There, the Court found no written description for claimed compounds that were defined only by their function — inhibiting the expression or activity of the PGHS-2 enzyme.

had no method of obtaining it and did not know any of its structural or physical properties. Finally, Noelle, just like the Regents, tries to rely on putative methods of production for written description of his compound claims. Noelle's argument, like that of the Regents, fails. As the *Lilly* Court ruled, methods do not provide written description for compounds. *Lilly*, 119 F.3d at 1567, 43 USPQ2d at 1405. *See also Fiers*, 984 F.2d at 1169, 25 USPQ2d at 1604-5.

The Board carefully considered the distinctions Noelle seeks to draw between the technology in this case and the facts in *Lilly*. The Board found those distinctions unpersuasive: "[l]ike *Lilly*, Noelle's claimed invention, as of February 14, 1992, involved an unpredictable technology. As with *Lilly,* Noelle presents a claim to a genus and to a particular species, human, while describing only one species (mouse)." JA00062.

2. Substantial Evidence Supports The Board's Findings Of Fact

a. Noelle Did Not Have Possession Of His Genus Or Human Claims

Noelle concedes "that a principal purpose of the written description requirement is to ensure that the applicant possessed the claimed invention as of the applicable filing date . . ." N.Br. 8. Noelle is, however, mistaken when he asserts that the Board confused possession of the claimed

invention with physical possession of an anti-human CD40CR antibody. N.Br. 8, 34.[5]

The Board properly followed the correct legal precedent that "[t]he inventor can demonstrate possession by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." JA00057, ll. 19-20. Further, the Board assessed Noelle's specification in its entirety. But, it found no description for the claimed human or generic mAbs or the non-mouse CD40CRs to which they bind. Without such description, there could be but one conclusion: Noelle did not possess any monoclonal antibody specific to a non-mouse CD40CR antigen, including anti-human CD40CR mAbs, or any non-mouse CD40CR antigen, including a human CD40CR antigen.

Nor did Noelle point to any common features that might have linked his disclosed anti-mouse CD40CR mAb and mouse CD40CR antigen

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[5] *Burroughs Wellcome Co.* v. *Barr Labs.*, 40 F.3d 1223, 1231, 32 USPQ2d 1915, 1921-22 (Fed. Cir. 1994) is of no help to Noelle. That case involved conception of an invention for methods of using a known compound. This Court held that reduction to practice is not necessarily required for conception in that case and distinguished *Amgen* and *Fiers* on the basis that, unlike conception of a DNA, methods of using and compositions comprising a ***known*** compound do not require knowledge of the structure of the compound. Here, neither human CD40CR antigen nor its antibodies were known compounds.

to the respective antibodies and antigens of other mammalian species. JA00063. As the Board held, "Noelle '480 does not describe the structure that is common to both mouse and human CD40CR that is essential for a common function of the two proteins." JA00049, ll. 12-4.

Finally, Noelle did not describe a representative number of species of CD40CRs or mAbs to that antigen. JA00540. On this basis also then, Noelle had no support for his generic claim.

As the Court in *Lilly* held: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, . . . falling with the scope of the genus. . . " *Lilly*, at 119 F.3d 1569, 43 USPQ2d 1405-6. Noelle has disclosed a single species -- a mAb to a mouse CD40CR. And, Noelle has pointed to nothing that suggests, as of February 14, 1992, that a person skilled in the art would expect CD40CR antigens to potentially exist in vertebrate species, ranging from mammals to fish and from lamprey to monkey. JA00535, ¶ 10; JA00536-7; JA04245-6, ¶ 26.

b. Noelle's Supposed Methods For Producing A MAb Specific To A Non-Mouse CD40CR Or For Producing A Non-Mouse CD40CR Antigen Do Not Satisfy The Written Description Requirement

Noelle apparently accepts, as he must, that his application does not describe any mAb, other than one (MR1) that binds to mouse CD40CR, or any CD40CR antigen (39kD) antigen other than mouse. As a supposed substitute for that lack of written description, Noelle attempts to create the impression that the necessary starting materials and methods were available to produce non-mouse CD40CR and mAbs to it. N.Br. 15-16; 26-27.[6] Noelle fails. His position is contrary to the law and the facts.

As this Court in *Fiers* said, methods of production are no substitute for written description. *Fiers*, 984 F.2d at 1169, 25 USPQ2d at 1604-5. *See also Lilly*, 119 F.3d at 1567, 43 USPQ2d at 1405. Further, none of the methods to which Noelle points would have led to the claimed

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[6] Noelle attempts to create the impression that it was Lederman who first raised the issue of methods and, thus, led the Board to confuse written description and enablement. N.Br. 16, n.3. Noelle is mistaken. Lederman had no reason to talk about methods. It was Noelle who first pointed to methods in a failed attempt to save his application from its failure to provide a written description for the claimed human antibodies. *See, e.g.*, N.Br. 15-16, 27.

non-mouse mAbs or to the CD40CRs to which they bind with a reasonable expectation of success.

Contrary to Noelle's contentions about the potential sources of a human CD40CR antigen, his application does not disclose that human CD40CR is expressed "specifically on human T-cells." N.Br. 14-15. Noelle's cited support for this incorrect proposition (JA00336 at § 6.2.3) shows only that mouse CD40CR antigen is expressed on activated mouse T cells. There is no evidence that the same is true for human cells. Indeed, the Board found that differences between regulation of human and murine B cells make it difficult to extrapolate the results obtained from one system to another. JA00012. The other two citations (JA00324, ll. 5-8 and JA00339, § 7) pointed to by Noelle also do not demonstrate that a human CD40CR antigen is present on any human T cell.

Wholly apart from whether or not activated human T cells actually display a human CD40CR on their surface, there can be no dispute that many other antigens also are displayed on the surface of those cells. As a consequence, as the Board correctly found: "[i]mmunization with activated human T cells or non-activated [human T cell] lines, such as Noelle's Jurkat and HSB2, would be expected to raise [antibodies to] a number of known and unknown T cell proteins, such as CD4, OX40 receptor, CD25, MHC

class II and ICAM-1." JA00012, ll. 8-10, internal citations omitted. Indeed, Noelle agrees. N.Br. 17. Yet, Noelle has provided no reagent or other means that would successfully screen the extensive population of different antibodies to isolate anti-human CD40CR antibodies. JA01770-1, ¶¶ 26-27.

Noelle also argues that his application describes the use of the CD40-Ig fusion protein for the characterization and purification of human CD40CR antigens. N.Br. 14-15. Not so. The Board correctly found that "construction of CD40-Ig fusion protein, such as Noelle's CD40-Ig, would have been extremely difficult." JA00048-9, ¶ 33. The Board also properly accorded little weight to Noelle's CD40-Ig binding experiments, which had no control and, thus, did not demonstrate that CD40-Ig actually bound to human CD40CR antigens. JA00050, ¶ 35; JA00063-4.[7] Finally, even Noelle did not use the CD40-Ig fusion protein of his application to isolate human CD40CR antigens or mAbs to them when he did that almost a year

[7] Noelle is mistaken that ". . . Lederman did not even try to prove [what the experiment in Section 7 might not have demonstrated]." N.Br. 29-30. Lederman provided ample proof that the results of Noelle's experiment needed to be carefully scrutinized. JA00573. In Noelle's experiment, "[a]bsent the proper control, one skilled in the art could not have known whether the CD40-Ig fusion protein was binding to a cell surface protein on Jurkat and HSB2 cells via the CD40 portion of the CD40-Ig molecule." JA00050, ¶ 35; JA00573, ¶ 39; JA00543, ¶ 30. The Ig portion, in contrast, is not capable of binding CD40CR. It may, however, bind to other compounds on the surface of the activated T cells. JA01767, ¶ 20.

after his earliest claimed filing date. Noelle first mutated the fusion protein to reduce the binding of the Ig portion of the fusion to the compounds, other than CD40CR, on the surface of the cells. JA01764, ¶ 14; JA01752, ¶ 32; JA1504-16 at JA01510, right col. ll. 17-20.

In the case of the human CD40CR antigen, Noelle's "methods of production", thus, fail on two counts. They do not demonstrate that Noelle's purported source of human CD40CR antigen -- activated human T cells -- is in fact such a source. And, they fail to provide a reagent for isolating human CD40CR antigen from the diverse population of antibodies that are necessarily produced from activated T cells.

c. Description Of The General Function Of An Antibody -- It Binds To An Antigen -- Does Not Satisfy The Written Description Requirement

Noelle's description of anti-CD40CR antibodies by their ability to bind to a CD40CR antigen is not written description. JA00063. Noelle has not identified either the antibody or the antigen. His functional description is nothing but a statement of the general dogma of the antigen-antibody relationship. Noelle's "definition" is also is circular and thus meaningless. Nor does it distinguish the claimed mAbs from any other mAbs. All bind to their antigens. JA00040, ¶ 9.

As this Court held in *Amgen*:

> It is not sufficient to define [a compound] solely by its principal biological property . . . because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

Amgen, 927 F.2d at 1206; 18 USPQ2d at 1021 (Fed. Cir 1991).

Noelle's arguments about the supposed long-established practice of antibody definition-by-function at both the judicial and Patent Office levels are of no help to him. N.Br. 9, 32-4. In all of those cases, the antigen was identified and available.[8] Here, no human CD40CR antigen was available. Noelle has described no CD40CR, other than mouse.

Indeed, the Synopsis of Applications of Written Description Guidelines[9] of the United States Patent and Trademark Office ('Guidelines") regarding antibodies support Lederman, not Noelle. JA03896A-JA03961 at JA03954-5.

In particular, Example 16 of the Guidelines makes plain that, **when an antigen has been isolated and purified**, a claim to an antibody

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[8] *See, e.g., In re Wands*, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988) (hapatitis B surface antigen); *Ex parte Erlich*, 22 USPQ2d 1463 (Bd. Pat. App. & Inter. 1992) (IFN-β); *Staehelin* v. *Secher*, 24 USPQ2d 1513 (Bd. Pat. App. & Inter. 1992) (IFN-α). *See* N.Br. 9, 31, 33.

[9] This Court in *Enzo* cites with approval sections of these Guidelines. *Enzo*, 323 F.3d at 964-7, 63 USPQ2d at 1612-5.

that binds to it is appropriate. JA03954-5. The Guidelines also explain why that claim is proper -- "method[s] of making antibodies to **fully characterized antigens**" are routine (emphasis added). JA 03955. Noelle has not isolated and purified any CD40CR antigen, except mouse. Nor has he fully characterized any non-mouse antigen.

No doubt in certain situations, "*. . . functional characteristics . . . coupled with a known or a disclosed correlation between function and structure*" suffices for written description of an invention. *Enzo,* 323 F.3d at 964, 63 USPQ2d 1612 (Fed. Cir. 2002) (internal citation omitted). N.Br. 34. Such situations are, however, inapposite to the facts here.

Noelle has not described either member of any antibody-non-mouse-antigen binding pair. He has not isolated and has not distinguished by any physical or structural features a mAb to any non-mouse CD40CR. He has not isolated or distinguished by any physical or structural characteristics any non-mouse CD40CR antigen. Both members of Noelle's non-mouse binding pair are, thus, unidentified and not distinguished from other compounds. One unidentified compound cannot define another. And, this is true even for antigens and antibodies. See *Johns Hopkins* v. *CellPro*, 931 F. Supp. 303, 321 (D. Del. 1996) ("[O]ne skilled in the art cannot make

an antibody to an unknown antigen"), *aff'd in part, vacated in part*, 152 F.3d 1342, 47 USPQ2d 1705 (Fed. Cir. 1998).

Noelle contends that this case is about functionally describing an antibody, not about providing the antigen that binds to the antibody.[10] According to Noelle, the Board improperly focused on the absence of structural or sequence information concerning non-mouse CD40CR antigens. Noelle then asserts that the Board erred because Noelle's claims are not directed to CD40CR antigens, but to anti-CD40CR antibodies. Noelle also contends that the experts agreed that neither sequence nor structural information for a CD40CR antigen was necessary to generate antibodies to it. N.Br. 28. Noelle is wrong.

As the Guidelines (*supra*, pp. 33-34) and *CellPro* make plain, to claim an antibody, based on its binding to an antigen, the antigen must be available. Yet, Noelle's application has provided only the mouse CD40CR antigen (a 39kD protein). It specifically binds to mouse mAb MR1. It does not bind and cannot produce any non-mouse mAb.

As the Board correctly found:

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[10] The structure of antibodies that bind different antigens are not the same. JA00038; JA00553.

> . . . the skilled artisan could not have predicted with any reasonable degree of certainty from Noelle's disclosure whether particular CD40CRs . . . could be generated and isolated other than Noelle's disclosed mouse CD40CR. . . . Indeed, it would have been difficult for the skilled artisan to generate and isolate the CD40CRs and antibodies specific to the CD40CRs . . . beyond those disclosed by Noelle's application.

JA00048, ¶ 32 (internal citations omitted; emphasis in original).

And, as the Board also correctly found, "differences between the regulation of human and murine B cells make it additionally difficult to extrapolate the results obtained from one system to another." JA00012, ¶ 43 (internal citation omitted).

Further, while "[a]ntibodies have long been described by their binding specificities, and not by their amino acid sequences, their chemical formulas, their molecular weights or other physical or chemical characteristics" (N.Br. 9, ll. 4-6), there can be no meaningful description if the substance (the antigen) to which the claimed antibody binds is not provided or identified by structure or physical characteristics.

Noelle's reliance on Dr. Shevach, one of Lederman's experts, is also to no avail. N.Br. 9, citing JA02580-6; N.Br. 19. Dr. Shevach never testified that a skilled artisan at the relevant time could make a mAb to a unknown antigen without undue experimentation. To the contrary, Dr. Shevach stated that "[a person skilled in the art] would consider the

production of monoclonal antibodies to an unidentified, uncharacterized antigen to be unpredictable -- requiring far from routine experimentation." JA00555. Dr. Kelsoe, Lederman's other expert, agreed. JA00540-1, ¶ 24.

C. The Board Correctly Found That Noelle's Human And Genus Claims Were Anticipated By The Prior Art

Noelle admits that, if his human and genus claims lack written description in the '799 application (which they do), and therefore, are not entitled to the benefit of the February 14, 1992 filing date of that application (which they are not), the prior art anticipates those claims under 35 U.S.C. § 102(b). N.Br. 4.

D. The Board Correctly Held That There Was No Interference-in-Fact Between Noelle's Mouse Claims And Lederman's Human Claims

Noelle challenges the Board's ruling of no interference-in-fact between Noelle's mouse claims and Lederman's human claims. N.Br. 39. There are two prongs to Noelle's argument. Both fail.

In the first prong of his argument, Noelle contends that the Board applied the wrong legal standard -- the two-way obviousness test. N.Br. 39. Noelle says that the one-way distinctiveness test is the correct standard. N.Br. 40. Noelle also contends that the Board failed to place the burden on Lederman to show that his anti-human CD40CR monoclonal

antibodies were both novel and non-obvious over Noelle's anti-mouse CD40CR monoclonal antibodies. N.Br. 40.

Noelle is wrong on both counts. The Board assessed interference-in-fact using two one-way tests. Either was sufficient to find in Lederman's favor. One looked from mouse to human. The other looked from human to mouse. And, in both directions, the Board placed the burden on Lederman, the moving party:

> ***Mouse* to *Human***
>
> . . . Lederman has demonstrated that one skilled in the art, provided with Noelle's "mouse" claims and the prior art, would not have had a reasonable expectation of success of obtaining the anti-human antibodies. Accordingly, we hold that Lederman has sufficiently established that its "human" are not obvious or anticipated by Noelle's "mouse" claims. As such, no interference-in-fact exists between Noelle's remaining patentable claims[11] and Lederman's claims.

JA00004. This test -- mouse to human -- is exactly the one Noelle argues the Board should have used. N.Br. 40. It did. Noelle has nothing to complain about. Noelle's argument about one way distinctiveness or two

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[11] In the *Noelle* v. *Armitage* interference (the subject of Appeal No. 03-1361 before this Court), the Board apparently ruled that all of Noelle's mouse claims are unpatentable to him based on lack of enablement. JA04188-211.

way patentability is moot. Human is patentable over mouse. There is no infringement-in-fact.

Human* to *Mouse

> Likewise, we conclude that one skilled in the art would have lacked a reasonable expectation of success of obtaining Noelle's claimed "mouse" subject matter when provided with Lederman's claimed "human" subject matter using those same screening methods. Additionally, we find that the alleged "similarity" in size does not help Noelle.

JA00027.

In the second prong of his argument, Noelle asserts that the Board erred in "refus[ing] to consider relevant evidence on the issue of expectation of success contained in Noelle's specification." N.Br. 11, 39. In particular, Noelle points to the Board's refusal to consider that portion of Noelle's specification that relates to the use of CD40-Ig fusion protein as a supposed reagent to obtain a human CD40CR antigen. N.Br. 50. Noelle is wrong. The Board applied the correct legal standard in assessing the prior art.

It is the parties' *claims*, not their specifications, on which a no interference-in-fact determination is made. It is the claims that define the interfering "invention". Rule 1.601(j) and (n) make this plain:

> An interference-in-fact exists when at least one *claim* of a party that is designated to correspond to a count and at least one

> *claim* of an opponent that is designated to correspond to the count define the same patentable invention.

37 C.F.R. § 1.601(j) (2002) (emphasis added).

> Invention "A" is the same patentable invention as invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

37 C.F.R. § 1.601(n) (2002).

And, as recognized by the Board, the parties' claims *are not* directed to methods for producing monoclonal antibodies or to Noelle's CD40-Ig fusion protein. JA00019. They are directed to mAbs to mouse (Noelle) or human (Lederman) CD40CR. Thus, CD40-Ig is not an element of Noelle's mouse claims.[12] It need not be considered in assessing no interference-in-fact.

Certainly, as the Board acknowledged, the specification may be "relied upon to serve as a dictionary for the terms appearing in the claims or for admissions against interest against prior art." JA00019. What Noelle urges, however, is much more. Noelle wants to supplement the prior art with another invention, unrelated to an anti-mouse CD40CR mAb, when

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[12] In fact, United States patent 6,472,510 issued from Noelle's '975 application (the immediate parent of the Noelle '480 application in interference) on October 29, 2002. The claims of that patent are directed to Noelle's CD40-Ig fusion protein. JA04212-33, *see, e.g.*, claim 5.

assessing the patentability of Lederman's anti-human CD40CR mAb. Noelle's position is contrary to the law.

Winter v. *Fujita*, 53 USPQ2d 1234, 1245 (Bd. Pat. App. & Inter. 1999) does not support Noelle. N.Br. 47. The *Winter* Board analyzed interference-in-fact based on the parties' claims. To interpret Fujita's catalyst claim 8, which contained a use limitation -- "use for polymerization of olefins" -- the Board turned to Fujita's specification to construe that use, *i.e.*, it used the specification for definitional purposes only. *Winter*, 53 USPQ2d at 1244-5.

Even were Noelle's view of the role of the specification in the assessment of no interference-in-fact to be correct (which it is not), substantial evidence would still support the Board's decision of no interference-in-fact.

As we will demonstrate, Noelle's CD40-Ig cannot be used with a reasonable expectation of success to isolate a human CD40CR antigen. *See infra*, p. 44.

1. Lederman's Anti-Human CD40CR MAb Would Not Have Been Obvious In View Of Noelle's Anti-Mouse CD40CR MAb[13] –

For an invention to be obvious, the prior art must provide two things. It must provide a motivation to make the claimed invention and it must provide a reasonable expectation of success in doing so. *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

The parties agree that the skilled artisan would have been motivated to obtain the anti-human CD40CR antibody, if the anti-mouse CD40CR antibody were available in the prior art. JA00014. Despite that motivation, however, the skilled worker would have no reasonable expectation of success in preparing or isolating an anti-human CD40CR mAb in view of the assumed preparation or isolation of an anti-mouse CD40CR mAb.

First and foremost, Noelle's anti-mouse CD40CR mAb does not bind human CD40CR antigen and therefore it is of no help in identifying, isolating or purifying that antigen -- a critical starting material for preparing a mAb to human CD40CR.

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[13] The parties agree that Lederman's CD40CR mAb would not anticipate Noelle's anti-mouse CD40CR mAb, and vice versa. JA00013, ¶ 1.

Noelle does not even argue that his anti-mouse CD40CR antibody would be of any use to that end. Rather, Noelle proposes other methods of preparing the claimed mAb. None of these methods provides the required reasonable expectation of success. The Board's findings in this regard are supported by substantial evidence.

In order to make a mAb to a human CD40CR antigen with a reasonable expectation of success, a source of antigen and a way to identify the antibody produced from it are required. JA03868-96 at JA03875. Each of Noelle's proposed methods fails one or both of these requirements.

a. There Was No Reasonable Expectation Of Success Because No Source Of A Human CD40CR Antigen Was Available

Some of Noelle's supposed methods require a source of human CD40CR antigen. No such source existed.

Noelle suggests using CD40CR-expressing cells as a source of CD40CR antigen. This is futile. As the Board found "one skilled in the art would not have a reasonable expectation of success of identifying the activated T cells that produced the required CD40CR antigen or of isolating the antigen itself." JA00023.

There also was no method available to distinguish cells that expressed human CD40CR antigen from those that did not.

Noelle contends that the CD40-Ig fusion protein could be used to select cells that produce CD40CR. Noelle is wrong on the facts and the law. As we have already explained, Noelle's CD40-Ig cannot be used to supplement the prior art in the no interference-in-fact patentability determination. That fusion protein was only described in Noelle's pending application. It was not part of the prior art.

Even if Noelle's CD40-Ig were part of the prior art (which it is not), the skilled worker would not have been able to isolate a human CD40CR antigen with a reasonable expectation of success using the CD40-Ig. First, there was no reasonable expectation of even making the CD40-Ig fusion protein. The evidence on this was clear. Production of the fusion portion would have been extremely difficult. JA00008-9, Fact 33.

Furthermore, the Board found no evidence that Noelle's CD40-Ig even bound to a human CD40CR. JA00009, Fact 35; JA01761-7; JA01770-1, ¶¶ 26-7. While Noelle argues that CD40-Ig binds to human T cells, he never showed that it binds to a CD40CR antigen, to the extent that antigen even exists on those cells. There was no control in Noelle's experiment. JA00009, Fact 35. Even Noelle's expert, Dr. Clark agreed that a control should have been used. JA03501, ll. 12-13. Yet, without a control, there is no evidence that the purported binding of the CD40-Ig to the T cell

is through the CD40 portion, rather than the Ig portion. Nor is there any evidence, if the binding was through the CD40 portion, that the ϵD40 bound only to the CD40CR, to the extent it was even present on the T cell. JA00005. As a result, the Board correctly found: "[o]ne skilled in the art . . . would have doubts regarding the validity of Section 7 [of the application]." JA00009. Indeed, Noelle admitted that even he had no evidence that his CD40-Ig fusion protein actually bound a human CD40CR antigen:

> [D]id we ever take and isolate CD40CR -- or does nor application? Let's put it that way. Does our application ever do that, or did we ever put in proof that what this human CD40-Ig was binding to was the material that we thought it was? No.

JA4105-6 at JA4106.

For all of these reasons, the Board properly found that "the isolation and purification of . . . [CD40CR] was *not* a predictable art." JA00008, ll. 6-7.

b. There Was No Reasonable Expectation Of Success Because No Method To Identify And Isolate A MAb To Human CD40CR Antigen Was Available

Others of Noelle's methods require a method to identify and isolate a mAb to a human CD40CR antigen. No such method existed.

Noelle's +/- screening provides no reasonable expectation of success in obtaining an anti-human CD40CR mAb. JA3568-JA3896 at JA3885; JA00023. It only identifies antibodies that bind to antigens on activated, but not on non-activated, T cells. JA00023; JA03868-96 at JA03885. Many antigens, in addition to CD40CR, are present on activated, but not on resting, T cells. JA00023.

Noelle's functional screening method (N.Br. 18) also does not provide a reasonable expectation of success in obtaining an anti-human CD40CR mAb. JA01771. There is no evidence that an antibody that binds to a T cell and inhibits B cell activation is an antibody to human CD40CR antigen. Many other proteins on the surface of B cells and T cells are involved in the immune response. JA01770, ¶ 26.

Finally, Noelle's expression cloning method provides no reasonable expectation of success. As the Board found: "[a]s of February 14, 1992, it would have been difficult for one of ***ordinary*** skill in the art to conduct the expression cloning methodology recited in the Noelle '480 application." JA00009, Fact 36 (emphasis in original and internal citations omitted).

2. Noelle's Anti-Mouse CD40CR MAb Would Not Have Been Obvious In View Of Lederman's Anti-Human CD40CR MAb

The Board correctly found that Lederman's anti-human CD40CR antibody did not make Noelle's anti-mouse CD40CR antibody patentable. Substantial evidence supports the Board's holding.

For the same reasons that mouse does not make human obvious, human does not make mouse obvious.[14] At Lederman's filing date, there was no source of mouse CD40CR. And, at that date, there was no method to identify and isolate a mAb to the mouse antigen.[15]

E. The Board Properly Exercised Its Discretion To Forego A Priority Determination When No Noelle Claim Defines The Same Patentable Invention As Any Lederman Claim

Noelle argues, for the first time on appeal, that 35 U.S.C. § 135(a) requires the Board, irrespective of its decision of no interference-in-

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[14] There is no dispute that Lederman does not disclose the CD40-Ig fusion protein. Therefore, even if Noelle is right (which he is not) and the specification of the "interfering" application must be considered part of the prior art, CD40-Ig cannot be used to supplement Lederman's disclosure of human CD40CR antigen and the mAb that binds to it.

[15] The parties are in agreement that Lederman's human mAb does not anticipate Noelle's mouse mAb. The structures of the two antibodies are different, as evidenced by their very different binding specificities.

fact, to determine priority of invention. N.Br. 37-38.[16] Having failed to raise this issue before, Noelle should not be heard now. In any event, the Board committed no error.

The Board did exactly what the rules require. It took up the preliminary motions in the appropriate order. 37 C.F.R. § 1.640(b) (2002). ("An administrative patent judge may take up motions for decision in any order, may grant, deny, or dismiss any motion, and may take such other action that will secure the just, speedy and inexpensive determination of the interference.").

The Board first addressed Lederman's motion for unpatentability of Noelle's genus and human claims. This procedure was in accord with *Brenner* v. *Manson*, 383 U.S. 519, 86 S.Ct. 1033 (1966). In *Brenner*, the Supreme Court held that a determination that each party's claims are patentable is a precondition to an interference. *Id.* at 383 U.S. at 528, n.2, 86 S.Ct. at 1038, n.2.

After finding Noelle's genus and human claims unpatentable, the Board then considered Lederman's motion for no interference-in-fact.

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[16] A necessary predicate to Noelle's argument is that his human or genus claims are patentable to him. N.Br. 37. They are not. Hence, Noelle's assertions fall like a house of cards.

This procedure was in accord with *Berman* v. *Housey*, 291 F.3d 1345, 1354, 63 USPQ2d 1023, 1029-30 (Fed. Cir. 2002). In *Berman*, this Court cited with approval the Board's statement in *Gluckman* v. *Lewis* that "prudence will ordinarily counsel a schedule that focuses on the allegation of no interference-in-fact . . . ." 59 USPQ2d 1542, 1543-44 (Bd. Pat. App. & Inter. 2001).

Finding no interference-in-fact between the only remaining claims of each party, the Board was correct to terminate the interference without reaching the issue of priority. Interferences determine priority of inventions defined by ***claims***. Noelle had no claim remaining in his application that defined the same patentable invention as Lederman's human claims. Thus, the Board was right to enter judgment without determining priority. The Board's procedure was fully in accord with the requirements of 35 U.S.C. § 135(a): "The Board . . . shall determine questions of priority of the *inventions* . . . (emphasis added)" Here, there were no common inventions in need of a priority determination.[17]

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[17] If Noelle believed that his application supported some claim that was patentable to Noelle and that was interfering with Lederman's human claims, he should have moved to add it to the interference. Having failed to so move, Noelle cannot rewrite his claims on appeal and argue priority to them by pointing to some nebulous "invention." N.Br. 38.

Finally, contrary to Noelle's assertion, this Court has never held that the Board ***must*** address priority in an interference. To the contrary, this Court has explained that its decisions in *In re Gartside*, 203 F.3d 1305, 53 USPQ2d 1769 (Fed. Cir. 2000); *Guinn* v. *Kopf*, 96 F.3d 1419, 40 USPQ2d 1157 (Fed. Cir. 1996) and *Perkins* v. *Kwon*, 886 F.2d 325, 12 USPQ2d 1308 (Fed. Cir. 1989) stand for the proposition that "if . . . an issue of priority or patentability is fairly raised and fully developed on the record, then the Board has the *authority* to consider the issue even after the Board determines that one party was not entitled to its claims." *Berman*, 291 F.3d at 1352, 63 USQ2d at 1028 (Fed. Cir. 2002) (emphasis added).

Thus, while the Board has the authority to address priority, it is not compelled to do so. And, in this case, this Court's other pre-condition to a priority determination is also not fulfilled. As Noelle acknowledges, "the priority issues were not fully developed before the Board, . . ." N.Br. 38. In fact, no priority cases were submitted or cross-examined by either party.

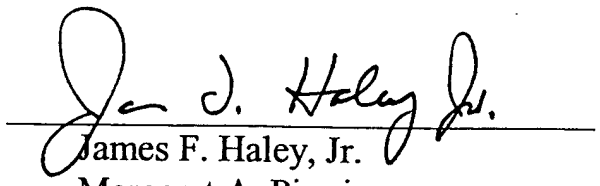
VI. CONCLUSION

In light of the foregoing, Lederman respectfully submits that the Board's determination that Noelle's February 14, 1992 priority application lacks written description, as required by 35 U.S.C. § 112, ¶ 1, for Noelle's genus and human claims should be affirmed.

Lederman also respectfully submits that the Board's determination that there is no interference-in-fact between Lederman's human claims and Noelle's mouse claims should be affirmed.

May 23, 2003

Respectfully submitted,



James F. Haley, Jr.
Margaret A. Pierri
Jane T. Gunnison
FISH & NEAVE
1251 Avenue of the Americas
New York, New York 10020
Tel.: (212) 596-9000
Fax.: (212) 596-9090

John P. White
COOPER & DUNHAM LLP
1185 Avenue of the Americas
New York, New York 10036
Tel.: (212) 278-0400
Fax.: (212) 391-0525

Attorneys for Appellees
Seth Lederman, Leonard Chess,
and Michael J. Yellin

CERTIFICATE OF SERVICE

I, Margaret A. Pierri, hereby certify that on May 23, 2003, I caused the original and eleven copies of the enclosed:

BRIEF OF APPELLEES SETH LEDERMAN, LEONARD CHESS, and MICHAEL J. YELLIN

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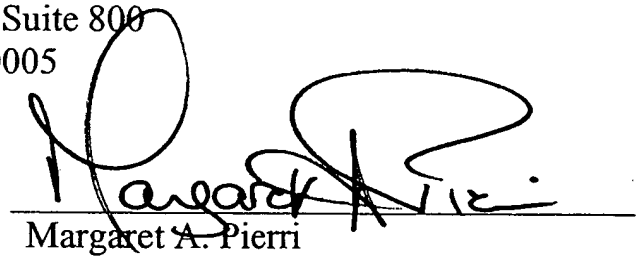
U.S. COURT OF APPEALS FOR THE FEDERAL CIRCUIT
717 Madison Place N.W.
Washington, D.C. 20439
Tel.: (202) 633-6550 Fax: (202) 633-9623

I further certify that I caused two copies of the enclosed to be sent by Federal Express (Airbill No. 8235 9104 3725) for Saturday delivery to attorneys for appellant:

E. Anthony Figg
Glenn E. Karta, Esq.
ROTHWELL, FIGG, ERNST & MANBECK
1425 K Street, N.W., Suite 800
Washington, D.C. 20005
Tel: (202) 783-6040
Fax: (202) 783-6031



Margaret A. Pierri
Attorney for Appellees Seth Lederman, Leonard Chess and Michael J. Yellin
FISH & NEAVE
1251 Avenue of the Americas
New York, New York 10020-1104
Tel.: (212) 596-9000
Fax: (212) 596-9090

CERTIFICATE OF COMPLIANCE

I, Margaret A. Pierri, hereby certify pursuant to Rule 32(a)(7)(C), Fed. R. App. P., that the word count measured by the word-processing system used to prepare this brief is 9916.

Margaret A. Pierri